Intramolecular Diels–Alder additions to 2-benzopyran-3-ones; anti-selectivity induced by the phenylsulfonyl group[1]

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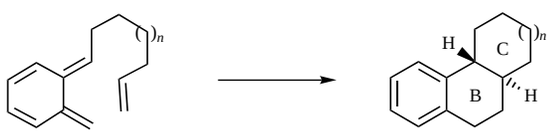
Intramolecular Diels–Alder additions of the 2-benzopyran-3-ones 2d, 2e and 2f with an *E*-SO_2Ph substituent on the dienophile (X = SO_2Ph in 2) show greatly enhanced *exo*-addition of the tether than is shown in the absence of the *E*-SO_2Ph group (X = H in 2). For 2e and 2f, *exo*-chain addition becomes preferred, and for 2d, *endo*-chain addition much less preferred, than in related cases with X = H. An *E*-CO_2Me group on the dienophile is also effective in enhancing *exo*-chain addition, but less effective than an *E*-SO_2Ph group. The adducts 4e and 4f undergo reductive elimination (5% Na–Hg) to give the diterpene related products 32 and 33 respectively.

Although simple *o*-quinodimethanes like **1** (*n* = 0 or 1) undergo predominant *exo*-selective Diels–Alder reactions to give *trans*-BC fused products (Scheme 1),[2] we found that related addition



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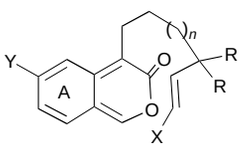
Scheme 1

in 2-benzopyran-3-ones **2** (X = H) gave mostly the product **3** of *endo*-chain addition (Scheme 2).[1b]

The products **3** with a *cis*-BC ring fusion were unsuitable for the synthesis of pisiferic acid **5**[3] and related diterpenoids (*e.g.* carnosol[4] and taxodione[5]) which had been one of our goals in exploring the intramolecular Diels–Alder (IMDA) reactions of 2-benzopyran-3-ones.[1b] The different behaviour of **1** and **2** is most simply attributed to repulsion between the bridging −C(O)O− moiety in **2** and an *exo* oriented tether. Moreover, steric clash with the pyrone ring A must be less significant than that with the −C(O)O− group.† This agrees with theoretical calculations on the addition of butadiene to ethylene[8] which suggest a product-like transition state rather than a parallel planes approach of the diene and dienophile. As a consequence there is closest approach between an *exo* directed hydrogen on the ethylene and the proximate *Z*-hydrogen of the diene. Whilst the detailed geometry of the Diels–Alder transition state will no doubt vary with the substituents on the diene and dienophile it seems likely that interaction between an *exo*-dienophile substituent and the proximate *Z*-substituent on the diene will remain an important factor in determining *endo–exo* selectivity. Accordingly we argued that if group X in **2** was bulky, its steric clash with the −C(O)O− moiety in an *endo*-chain addition would favour an *exo*-chain, *endo*-X transition state. It is noteworthy that in simple decatrienes **6** (Scheme 3) in which the *Z*-positions of the diene are occupied by hydrogens, a bulky *E*-SO_2Ph group on the dienophile favours the *exo*-position pre-



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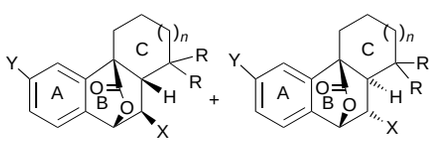
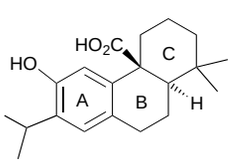


3 (major X = H) **4** (minor X = H)

	Y	R	X	*n*
a	OMe	Me	H	1
b	H	H	H	1
c	H	H	H	0
d	H	H	SO_2Ph	0
e	OMe	H	SO_2Ph	1
f	OMe	Me	SO_2Ph	1
g	OMe	H	CO_2Me	1

Scheme 2



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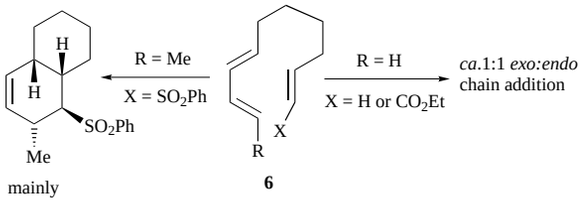
sumably due to greater steric interaction with the diene C-2–C-3 moiety in an *endo*-SO_2Ph (*exo*-chain) transition state.[9] This is a useful way of diverting the evenly balanced *endo–exo* (chain) preference in the IMDA reactions of decatrienes to obtain mostly *cis* ring fused products (Scheme 3) *i.e.* to achieve the opposite stereoselectivity to that required in the additions of the pyrones **2**.

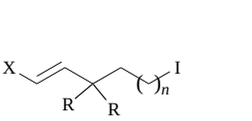
Because of its bulk and anticipated easy removal we chose the phenylsulfonyl group as X in an attempt to divert the

† The preferred *endo*-chain additions observed when X = H echoes the strong *endo*-selectivity in the addition of cyclopentene to the parent 2-benzopyran-3-one.[6] In both the intramolecular and the intermolecular reactions repulsion involving the lactone C(O)O group is one important factor. The existence of a second factor favouring *endo*-addition is suggested by the *endo*-preference observed for addition of *E*-α-cyano- and *E*-α-methoxycarbonyl-*o*-quinodimethane to cyclopentene. This other factor may be a secondary MO–MO interaction (steric attraction).[7]

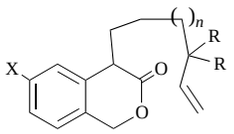


Scheme 3

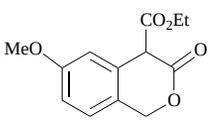
stereochemistry of IMDA addition within the pyrones **2a–c**. Several routes were used to prepare the precursors (*o*-formylphenylacetic acids) required to generate the pyrones **2** (X = SO_2Ph). Alkylation of 6-methoxyisochroman-3-one [KN($SiMe_3$)$_2$, THF–hexamethylphosphorous triamide (HMPT)] with the iodides **7a–c** gave mixtures of the required mono-alkylated products **8** with corresponding dialkylated products



7 a R = H, *n* = 2, X = H
b R = Me, *n* = 2, X = H
c R = H, *n* = 1, X = H
d R = H, *n* = 1, X = SO_2Ph



8 a R = H, *n* = 1, X = OMe
b R = Me, *n* = 1, X = OMe
c R = H, *n* = 0, X = OMe



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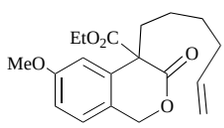

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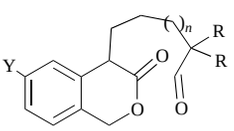
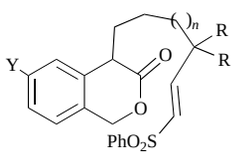
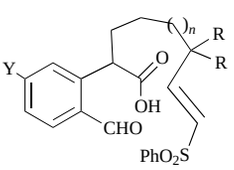


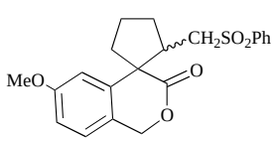
11 a R = H, *n* = 1, Y = OMe
b R = Me, *n* = 1, Y = OMe
c R = H, *n* = 0, Y = OMe



12 a R = H, *n* = 1, Y = OMe
b R = Me, *n* = 1, Y = OMe
c R = H, *n* = 0, Y = OMe



13 a R = H, *n* = 1, Y = OMe
b R = Me, *n* = 1, Y = OMe
c R = H, *n* = 0, Y = H
d R = H, *n* = 1, Y = H



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that had to be removed by chromatography.[1b] An attempt to avoid dialkylation involved ethoxycarbonylation of 6-methoxyisochroman-3-one [(CO_2Et)$_2$, NaH, benzene, reflux] and gave **9** in 48% yield. Alkylation of **9** with **7a** gave **10** (64%) which was smoothly hydrolysed and decarboxylated to **8a** (95%). However the overall yield was inferior to that from direct alkylation of 6-methoxyisochroman-3-one (~50%).

Ozonolysis of the compounds **8a**, **8b** and **8c** gave the corresponding aldehydes **11a**, **11b** and **11c** which upon addition of $PhSO_2CH_2Li$ (THF, −78 °C) and dehydration of the resulting hydroxy sulfones ($MeSO_2Cl$, Et_3N, THF, −5 °C, 30 min) gave **12a**, **12b** and **12c**. For **12a** and **12b** lactone ring opening (K_2CO_3–H_2O–MeOH, reflux, 1 h), esterification with diazomethane and Swern oxidation then gave the methyl esters of the required acids **13a** and **13b**. The acids were than obtained by hydrolysis (K_2CO_3–H_2O–MeOH, reflux, 1 h).

An attempt to open the lactone ring in **12c** foundered due to a more rapid intramolecular Michael addition. After a work-up involving acidification at 0–5 °C and reaction with diazomethane, the *cis–trans* isomers corresponding to structure **14** were isolated as well as 24% of the desired hydroxy ester. This suggests faster closure of five- compared to six-membered rings *via* Michael addition although both these ring sizes are readily obtained *via* such additions.[10] In seeking other routes to structures like **13c** we found that the problem of dialkylation experienced with isochroman-3-ones [KN($SiMe_3$)$_2$, THF–HMPT)][1b] disappeared when the ethylene acetal of ethyl *o*-formylphenylacetate was alkylated with **7a** and **7c** under the same conditions; the monoalkylated products **16** and **17** were obtained in 60 and 53% yield respectively. Upon base hydrolysis these gave the ethylene acetals of acids **18** and **19** which readily underwent acid-catalysed hydrolysis to **18** and **19**. Reaction of the ethylene acetal of **19** with $PhSeSO_2Ph$ (irradiation with a water-cooled 125 W medium pressure mercury lamp)[11] and subsequent H_2O_2 oxidation–selenoxide elimination of the resulting selenosulfones gave the α,β-unsaturated sulfone **20**; acid hydrolysis then gave **13c**. In a related, but not identical, sequence ester **16** underwent selenosulfonation–selenoxide elimination to give the ethyl ester of **21** which underwent acetal hydrolysis (THF–HCl–H_2O), followed by ester hydrolysis (K_2CO_3–MeOH–H_2O), to give acid **13d**.

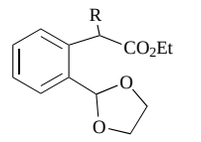
An attempt was made to introduce the intact α,β-unsaturated sulfone side chain by reacting **7d** with **15** [KN($SiMe_3$)$_2$, THF–HMPT]. The compound **7d** was prepared from the TBDMS ether of pent-4-en-1-ol using selenosulfonation–selenoxide elimination (see Experimental section). Unfortunately reaction of **7d** with **15** gave two products neither of which was the required mono-alkylation product. After hydrolysis of the acetal one product had ^{1}H NMR spectral characteristics consistent with structure **22** derived by Michael addition of the anion from **15** to give **23** followed by intramolecular displacement of iodide ion, as shown by the mechanism in **23**, and acetal hydrolysis. There are precedents for this behaviour involving α,β-unsaturated carbonyl compounds.[12] In the present case Michael addition to the α,β-unsaturated sulfone is clearly more rapid than S_N2 displacement of iodide.

The other product from this reaction does not have ^{1}H NMR spectral characteristics consistent with structure **24** derived from the desired product *via* intramolecular Michael addition (**25**; mechanism) and acetal hydrolysis. This product was subjected to careful chromatography but was never obtained completely pure. The high field resonances and proton–proton connectivity (COSY) shown by the product are consistent with structure **26**. Presumably **7d** is deprotonated and its anion undergoes rapid ring closure to the cyclopropane **27** which subsequently adds to the anion of **15** in a Michael reaction.

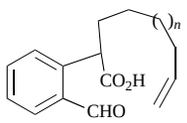
Reaction of the aldehyde **11a** with the sodium salt of trimethyl phosphonoacetate gave the α,β-unsaturated ester **28**. Upon lactone ring opening, acidification at 0–5 °C and methylation with diazomethane **28** gave the diester **29**. Swern oxidation gave the aldehyde **30** and a remarkably selective hydrolysis of this diester with K_2CO_3–MeOH–H_2O at 20 °C (1 h) gave the required aldehydo acid **31**.

In boiling acetic anhydride the acids **13a**, **13b** and **13c** underwent smooth dehydration to pyrones as indicated by the formation of yellow colours which faded with formation of the adducts of type **3** and **4**. As described in our earlier paper[1b] the ^{1}H NMR spectra of adducts of this type provide excellent evidence for their stereochemistry. The spectra upon which our current assignments are based are detailed in the Experimental section.

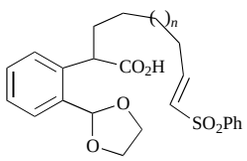
The ratios for *endo–exo* addition of the connecting chain observed for the compounds with an *E*-sulfonyl substituted dienophile are collected in Table 1 (entries 4–6) together with



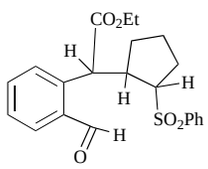
15 R = H
16 R = $(CH_2)_4CH{=}CH_2$
17 R = $(CH_2)_3CH{=}CH_2$



18 *n* = 1
19 *n* = 0



20 *n* = 0
21 *n* = 1



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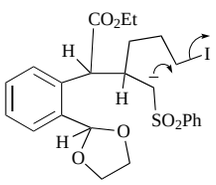

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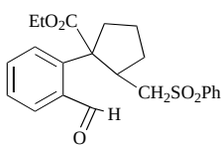

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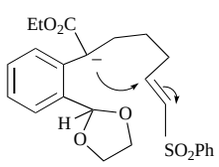

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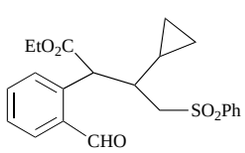

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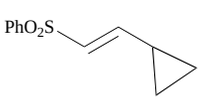

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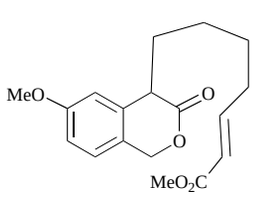

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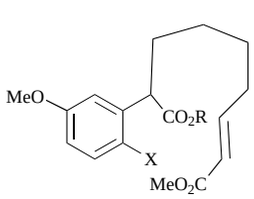


29 X = CH_2OH, R = Me
30 X = CHO, R = Me
31 X = CHO, R = H

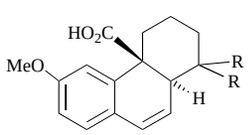
data for related compounds lacking the phenylsulfonyl group (entries 1–3). In entry 7 the effect of an *E*-CO_2Me group on the dienophile is determined. All ratios were obtained from well resolved ^{1}H NMR spectra (400 MHz) of the unpurified reaction product. Chromatographic isolation of the adducts agreed with these ratios. Yields in the reactions were usually >80%. It is clear that in all the cases examined the *endo–exo* (chain) ratio is much reduced in the *E*-SO_2Ph compounds. For the pyrones with *n* = 1 (four atoms in the tether) the *E*-SO_2Ph group gives mostly the *exo*-chain adduct whereas in the absence of the *E*-SO_2Ph group the *endo*-chain adduct is dominant (*cf.* entry 2 *vs.* 5 and entry 1 *vs.* 6). Entry 7 shows the *E*-CO_2Me group is somewhat less effective in inducing the same change in stereochemistry, suggesting a steric rather than a secondary MO–MO interaction effect for the sulfones.

Table 1

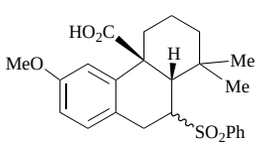
Entry	Pyrone	Ratio of *endo*:*exo* chain addition, **3**:**4**
1	**2a**	6.0:1
2	**2b**	4.5:1
3	**2c**	7.0:1
4	**2d**	1.4:1
5	**2e**	1.0:4.2
6	**2f**	1.0:2.6
7	**2g**	1.0:3.4

For the pyrones with three atoms in the tether (*n* = 0) the effect of introducing an SO_2Ph group is smaller but still well defined (entries 3 and 4). When the tether is longer (*n* = 1) the addition transition state is likely to involve greater synchrony of bond formation at the α and β positions of the α,β-unsaturated sulfone than when *n* = 0. In the latter case, bond formation at the β-carbon is likely to run ahead of that at the α-carbon. Consequently steric effects due to the SO_2Ph group at C-α will be less keenly felt in the transition state for the shorter tether.

Having served its purpose, the phenylsulfonyl group can be removed from **4e** and **4f** by treatment with 5% sodium–amalgam, when reductive β-elimination with the lactone in the manner of a Julia reaction provides the carboxylic acids **32** and **33** in good yield (>80%). In these cases the *trans* coplanar



32 R = H
33 R = Me



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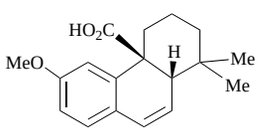

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arrangement of the eliminated groups leads to smooth reaction. In contrast, reaction of **3e** with sodium–amalgam gave mostly the saturated sulfone **34** (57%) and only 30% of the acid **35**. This failure is not of preparative significance as compounds like **35** are easily prepared *via* acid catalysed elimination of the readily available *endo*-chain adducts **3** (X = H).[1b]

In conclusion, we have shown that IMDA additions to 2-benzopyran-3-ones **2** allow preparation of either *cis*- or *trans*-fused hydrophenanthrenes related to natural diterpenoids. Our results may extend to other dienes linked between their termini. Such systems include important Diels–Alder dienes like cyclopentadienes, cyclohexadienes, furans, simple pyrones and other *o*-quinodimethanes. We also suggest that any diene with a *Z*-substituent will show an increased tendency to *endo*-addition of the larger group of a *trans*-dienophile in both inter- and intra-molecular addition. Indeed this may explain why *o*-quinodimethanes with a *Z*-cyano group break the general rule of *exo*-chain preference in IMDA additions to *o*-quinonoid dienes.[13]

Experimental

Mps were determined with a Kofler hot-stage apparatus and are uncorrected. Infrared spectra were recorded on a Philips PU 8706 infrared spectrophotometer, and referenced to a peak at 1601 cm^{-1} of polystyrene. Only significant absorbances are reported. Ultraviolet and visible spectra were recorded on a Pye-Unicam PU 8800 UV–VIS spectrophotometer; log ε values

are in parentheses. Unless otherwise stated ^{1}H NMR spectra were measured in $CDCl_3$ with tetramethylsilane as internal standard; 400 MHz NMR spectra were measured on a Bruker WH-400 instrument and 300 MHz spectra on a General Electric Nicolet QE 300 spectrometer. The position of NMR resonances are expressed in parts per million (δ), and coupling constants J are given in Hz. Mass spectra were obtained on an Autospec mass spectrometer. Chromatography on silica refers to short-column chromatography[14] over Kieselgel G60 (Merck). Thin layer chromatography was carried out on glass plates (15 × 5 cm^2), dipped in an ethyl acetate suspension of Kieselgel G60 and dried in an air oven at 120 °C for at least 1 h. Ether refers to diethyl ether and light petroleum to the fraction bp 60–80 °C. All solvents were distilled and dried before use by standard procedures.[15] Unless otherwise stated, all reactions were conducted under an atmosphere of dry, oxygen free argon. For procedures requiring anhydrous conditions all glassware was oven dried at 120 °C (18 h) prior to use. Solvents were removed under reduced pressure using a Buchi rotary evaporator at water pump pressure followed by heating on a steam bath at water pump pressure.

Ethoxycarbonylation of 6-methoxyisochroman-3-one

To a stirred solution of sodium hydride (1.27 g, of a 60% dispersion in mineral oil, 31.7 mmol) in benzene (20 ml) was added diethyl carbonate (2.65 g, 22.4 mmol) in benzene (5 ml). The reaction mixture was heated at reflux and a solution of 6-methoxyisochroman-3-one (2.0 g, 11.2 mmol) in benzene (16 ml) was added dropwise over 2.5 h and the reaction was heated at reflux (3 h). The contents of the flask were cooled to room temperature and glacial acetic acid (16 ml) was added dropwise followed by water (8 ml) and the reaction was stirred at 20 °C (15 h). The solution was poured into water, extracted with dichloromethane, dried ($MgSO_4$) and concentrated to give an oil (2.54 g). Chromatography on silica (80 g) eluting with dichloromethane gave the *ethyl* 6-*methoxy*-3-*oxochromane*-4-*carboxylate* **9** (1.34 g, 48%) (Found: C, 62.5; H, 5.7. $C_{13}H_{14}O_5$ requires C, 62.4; H, 5.6%); ν_{max}(film)/cm^{-1} 1750 and 1735; δ_H(300 MHz) 1.27 (3H, t, J 7.0, $CO_2CH_2CH_3$), 3.83 (3H, s, OMe), 4.21 (2H, m, $CO_2CH_2CH_3$), 4.63 (1H, s, methine-H), 5.20 (1H, d, J 13.5, benzylic-H), 5.60 (1H, d, J 13.5, benzylic-H), 6.88 (2H, m, Ar-H) and 7.16 (1H, d, J 8.0, Ar-H); *m/z* 250 (M$^+$), 193, 178, 177, 165, 149, 148, 121, 91 and 77 (15.4, 21.6, 29.4, 100.0, 19.2, 43.9, 27.6, 32.4, 21.1 and 21.3%).

Alkylation of 9 with 7a

To a stirred solution of **9** (116 mg, 0.46 mmol) in dry distilled DMF (5 ml) was added sodium hydride (21 mg, 0.53 mmol of a 60% dispersion in mineral oil) and the mixture was heated at 60 °C under argon (0.5 h). The solution was cooled to room temperature and a solution of the iodide **7a** (111 mg, 0.53 mmol) in DMF (2 ml) added. The mixture was heated at 55–60 °C (bath temperature) (16 h) then diluted with ether, washed with water (240 ml), dried ($MgSO_4$) and concentrated to give an oil. Chromatography on silica (32 g) eluting with dichloromethane gave *ethyl* 4-(*hex*-5-*enyl*)-6-*methoxy*-3-*oxochromane*-4-*carboxylate* **10** (98 mg, 64%) (Found: M$^+$, 332.1623. $C_{19}H_{24}O_5$ requires M^+, 332.1624); ν_{max}(film)/cm^{-1} 1740; δ_H(300 MHz) 1.19 (3H, t, J 7.0, OCH_2CH_3), 1.41 (2H, m), 2.01 (2H, q, J 7.0), 2.34 (2H, m), 2.47 (2H, m), 3.82 (3H, s, OMe), 4.15 (2H, q, J 7.0, OCH_2CH_3), 4.92 (2H, m, olefinic-H), 5.29 (1H, d, J 14.0, benzylic-H), 5.45 (1H, d, J 14.0, benzylic-H), 5.74 (1H, m, olefinic-H), 6.81 (1 H, s, Ar-H), 6.88 (1H, d, J 8.5, Ar-H) and 7.09 (1H, d, J 8.5, Ar-H); *m/z* 332 (M$^+$), 259, 249, 213, 204, 203, 173, 159, 145 and 41 (18.1, 53.4, 100.0, 60.1, 68.0, 98.8, 29.4, 36.3, 52.4 and 39.9%).

Hydrolysis of 10

The title compound (71 mg, 0.21 mmol), potassium carbonate (59 mg, 0.43 mmol), methanol (2.2 ml) and water (1.1 ml) were heated at 50 °C (bath temperature) (6 h). The mixture was acidified to pH 1 with dilute hydrochloric acid (2 mol dm^{-3}), extracted with ether, washed (water), dried ($MgSO_4$) and concentrated. The crude product was heated on a steam bath (100 °C) (10 min) to give the *decarboxylated product* **8a** (52 mg, 95%). The ^{1}H NMR spectrum of the product was identical to that of a previously prepared sample.[1b]

Preparation of the aldehyde 11a

The olefin **8a** (2.0 g, 7.69 mmol) was dissolved in dry dichloromethane (27 ml) and dry methanol (40 ml) and ozonolysed at −78 °C (0.5 h). Dry argon was bubbled through the solution (1 h) and dimethyl sulfide added. Then the solution was allowed to reach room temperature with stirring (3 h). Chromatography of the evaporated product on silica (40 g) in benzene–ether (7:3) gave 4-(5-*oxopentyl*)-6-*methoxychroman*-3-*one* **11a** (1.53 g, 76%) as an oil (Found: C, 68.9; H, 6.8. $C_{15}H_{18}O_4$ requires C, 68.7; H, 6.9%); ν_{max}(film)/cm^{-1} 2740, 1740 and 1730; δ_H(300 MHz) 1.54 (2H, m), 1.70 (2H, m), 1.87 (1H, m), 1.98 (1H, m), 2.49 (2H, t, J 7.0, methylene-H), 3.56 (1 H, t, J 7.0, methine-H), 3.83 (3H, s, OMe), 5.21 (1H, d, J 14.0, benzylic-H), 5.38 (1H, d, J 14.0, benzylic-H), 6.73 (1H, s, Ar-H), 6.82 (1H, dd, J 8.5 and 2.0, Ar-H), 7.14 (1H, d, J 8.5, Ar-H) and 9.77 (1H, s, CHO); *m/z* 262 (M$^+$), 177, 149, 83, 70, 57, 56, 55, 43 and 41 (29.3, 22.7, 22.7, 23.3, 23.5, 100.0, 22.7, 28.6, 36.9 and 42.2%).

Preparation of the aldehyde 11b

Ozonolysis of the previously described alkene **8b**[1b] in the manner described above and work-up as above gave 4-(4,4-*dimethyl*-5-*oxopentyl*)-6-*methoxychroman*-3-*one* **11b** (75%) as an oil (Found: M$^+$, 290.1507. $C_{17}H_{22}O_4$ requires M^+, 290.1518); ν_{max}(film)/cm^{-1} 1720 and 1740; δ_H(300 MHz) 1.05 (6H, s, 2 × Me), 1.46 (2H, m), 1.54 (2H, m), 1.86 (1H, m), 1.95 (1H, m), 3.55 (1H, t, J 7.0, methine-H), 3.82 (3H, s, OMe), 5.20 (1H, d, J 14.0, benzylic-H), 5.36 (1H, d, J 14.0, benzylic-H), 6.71 (1H, d, J 2.0, Ar-H), 6.81 (1H, dd, J 2.0 and 8.5, Ar-H), 7.13 (1H, d, J 8.5, Ar-H) and 9.44 (1H, s, CHO); *m/z* 290 (M$^+$), 180, 178, 177, 162, 159, 147, 121, 91 and 41 (59.6, 100.0, 53.7, 73.5, 49.7, 73.4, 49.4, 53.9, 54.4 and 67.8%).

Preparation of the α,β-unsaturated sulfone 12a from the aldehyde 11a

To a stirred solution of methyl phenyl sulfone (1.0 g, 6.3 mmol, 1.1 equiv.) in THF (28 ml) under argon at −78 °C was added dropwise by syringe *n*-butyllithium (3.95 ml of a 1.60 M solution in hexanes, 6.30 mmol) to give a colourless solution of the anion. After 10 min a solution of **11a** (1.50 g, 5.73 mmol) in THF (8 ml) was added *via* a cannula at −78 °C, rinsing with a further portion of THF (8 ml). After 2.5 h, the reaction was quenched by the addition of a solution of acetic acid in THF (7.5 ml of a 1.0 M solution, 1.3 equiv.). The mixture was then allowed to reach room temperature (1 h) and poured into a 1:1 mixture of dichloromethane and saturated aqueous sodium hydrogen carbonate (160 ml). The aqueous layer was extracted with CH_2Cl_2 (2 × 80 ml) and the combined organic layers were washed with water (3 × 80 ml), dried ($MgSO_4$) and concentrated under reduced pressure to give an oil. Chromatography of the oil on silica (310 g) in benzene–ether (3:7) gave the β-*hydroxy sulfone* as an oil (1.58 g, 66%) (Found: M$^+$, 418.1458. $C_{22}H_{26}O_6S$ requires M^+, 418.1450); ν_{max}(film)/cm^{-1} 3500 and 1735; δ_H(300 MHz) 1.46 (6H, m), 1.80 (1H, m), 1.93 (1H, m), 3.14–3.27 (2H, m), 3.42 (1H, m, OH), 3.53 (1H, t, J 7.0, methine-H), 3.82 (3H, s, OMe), 4.16 (1H, m), 5.19 (1H, d, J 14.0, benzylic-H), 5.37 (1H, d, J 14.0, benzylic-H), 6.70 (1H, s, Ar-H), 6.81 (1H, dd, J 8.5 and 2.0, Ar-H), 7.12 (1H, d, J 8.5, Ar-H), 7.65 (3H, m, SO_2Ph) and 7.94 (2H, SO_2Ph); *m/z* 418 (M$^+$), 213, 191, 178, 177, 161, 147, 121, 91 and 77 (54.7, 45.3, 48.3, 35.6, 100.0, 23.8, 26.8, 25.4, 26.6 and 58.2%).

To a stirred solution of the hydroxy sulfone (1.50 g, 3.59 mmol) in dry dichloromethane (40 ml) under argon at −6 °C

was added dropwise *via* syringe triethylamine (5.0 ml, 36.0 mmol, 10 equiv.) followed immediately by methanesulfonyl chloride (0.84 ml, 10.8 mmol, 3 equiv.). The reaction was then allowed to warm to room temperature (1 h). The mixture was poured into saturated aqueous ammonium chloride (75 ml) and extracted with dichloromethane (3 × 40 ml). The combined organic layers were washed with saturated aqueous ammonium chloride (2 × 75 ml) and then water (75 ml), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the crude product on silica (30 g) in benzene–ether (2:3) gave the 4-(6-*phenylsulfonylhex*-5-*enyl*)-6-*methoxychroman*-3-*one* **12a** as an oil (1.29 g, 90%) (Found: C, 66.0; H, 6.0; S, 7.7. $C_{22}H_{24}O_5S$ requires C, 66.0; H, 6.0; S, 8.0%); ν_{max}(film)/cm^{-1} 1735; δ_H(300 MHz) 1.53 (4H, m), 1.84 (1H, m), 1.95 (1H, m), 2.27 (2H, m), 3.53 (1H, t, *J* 7.0, methine-H), 3.82 (3H, s, OMe), 5.20 (1H, d, *J* 14.0, benzylic-H), 5.36 (1H, d, *J* 14.0, benzylic-H), 6.31 (1H, d, *J* 15.0, olefinic-H), 6.70 (1H, s, Ar-H), 6.82 (1H, dd, *J* 8.5 and 2.0, Ar-H), 6.98 (1H, dt, *J* 15.0 and 7.0, olefinic-H), 7.14 (1H, d, *J* 8.5, Ar-H), 7.54 (3H, m, SO_2Ph) and 7.88 (2H, m, SO_2Ph); *m/z* 400 (M^+), 372, 231, 230, 213, 177, 147, 121, 91 and 77 (14.0, 24.0, 32.5, 49.7, 44.0, 100.0, 21.6, 31.8, 28.0 and 40.3%).

Preparation of the α,β-unsaturated sulfone 12b

4-(4,4-*Dimethyl*-6-*phenylsulfonylhex*-5-*enyl*)-6-*methoxychroman*-3-*one* was obtained in 40% yield in the manner detailed above for **12a** (Found: C, 67.2; H, 6.8; S, 7.6. $C_{24}H_{28}O_5S$ requires C, 67.3; H, 6.5; S, 7.5%); ν_{max}(film)/cm^{-1} 1740; δ_H(300 MHz) 1.06 (6H, s, 2 × Me), 1.45 (4H, m), 1.79 (1H, m), 1.91 (1H, m), 3.51 (1H, t, *J* 7.0, methine-H), 3.83 (3H, s, OMe), 5.20 (1H, d, *J* 14.0, benzylic-H), 5.35 (1H, d, *J* 14.0, benzylic-H), 6.19 (1H, d, *J* 15.5), 6.70 (1H, s, Ar-H), 6.83 (1H, dd, *J* 2.0 and 8.5, Ar-H), 6.93 (1H, d, *J* 15.5), 7.14 (1H, d, *J* 8.5, Ar-H), 7.58 (3H, m, SO_2Ph) and 7.87 (2H, m, SO_2Ph); *m/z* 428 (M^+), 259, 258, 178, 177, 149, 125, 77, 69 and 41 (12.2, 21.6, 23.9, 26.0, 100.0, 31.5, 23.7, 40.6, 20.7 and 27.5%).

Preparation of vinyl sulfone 12c

Ozonolysis of previously prepared[1b] **8c** as described above for **8a** gave the aldehyde (62%) as a pale yellow oil after chromatography on silica in benzene–ether (7:3); δ_H 1.75–2.15 (4H, m), 2.55 (2H, m), 3.60 (1H, t, *J* 7.0, benzylic methine), 3.90 (3H, s), 5.20 (1H, d, *J* 14.0), 5.36 (1H, d, *J* 14), 6.82 (2H, m), 7.14 (1H, m), 7.42 (1H, m) and 9.79 (1H, s); *m/z* 248, 191, 175, 163, 159, 147, 145, 121 and 91 (64, 100, 33, 35, 31, 44, 63, 32 and 40%). This aldehyde was converted into the 4-(5-*phenylsulfonylpent*-4-*enyl*)-6-*methoxychroman*-3-*one* **12c** *via* the hydroxy sulfone as described above for the preparation of **12a** (*ca* 30% yield over two steps) (Found: $M^{\cdot+}$, 386.118. $C_{21}H_{22}O_5S$ requires *M*, 386.118); δ_H 1.54–2.05 (4H, m), 2.30 (2H, m), 3.52 (1H, t, *J* 7.0, benzylic methine), 3.80 (3H, s), 5.17 (1H, d, *J* 13.5), 5.30 (1H, d, *J* 13.5), 6.33 (1H, d, *J* 15.0, olefinic-H), 6.68 (1H, br s), 6.81 (1H, m), 6.95 (1H, dt, *J* 15.0 and 7.0, olefinic-H), 7.11 (1H, m), 7.54 (3H, m) and 7.85 (2H, m); *m/z* 386, 245, 217, 216, 199, 187, 177, 77 (16, 11, 39, 79, 55, 29, 100 and 27%).

Conversion of 12a into 13a

The sulfone **12a** (860 mg, 2.15 mmol), potassium carbonate (590 mg, 4.3 mmol), methanol (21.5 ml) and water (10.75 ml) were stirred at room temperature (3.5 h). The mixture was cooled to 0–5 °C (ice–water) and transferred to a separating funnel where ice cold dilute hydrochloric acid (50 ml, 2 mol dm^{-3}) was added. The precipitated acid was extracted into ether (0 °C) and immediately treated with diazomethane. Evaporation of the solvent left an oil which was dried ($MgSO_4$) and concentrated to give the crude *ester* (909 mg, 98%) (Found: M^+, 432.1581. $C_{23}H_{28}O_6S$ requires *M*, 432.1562); ν_{max}(film)/cm^{-1} 3480 and 1730; δ_H(300 MHz) 1.28 (1H, m), 1.48 (2H, m), 1.78 (1H, m), 2.19 (4H, m), 3.64 (3H, s, CO_2Me), 3.79 (3H, s, OMe), 3.94 (1H, t, *J* 7.5, methine-H), 4.67 (2H, m, benzylic-H), 6.27 (1H, d, *J* 15.0), 6.77 (1H, dd, *J* 2.5 and 8.5, Ar-H), 6.93 (2H, m), 7.26 (1H, d, *J* 8.5, Ar-H), 7.58 (3H, m, SO_2Ph) and 7.86 (2H, m, SO_2Ph); the OH signal was not recorded; *m/z* 432 (M^+), 231, 230, 213, 178, 177, 137, 121, 91 and 77 (2.5, 27.6, 39.7, 43.4, 26.1, 100.0, 43.4, 32.6, 24.9 and 40.7%). To a stirred solution of dimethyl sulfoxide (394 mg) in dry dichloromethane (5 ml) was added oxalyl chloride (0.32 g) in CH_2Cl_2 (1 ml) at −78 °C with stirring under argon. The solution was stirred (4 min) then the alcohol added dropwise (909 mg, 2.1 mmol) in CH_2Cl_2 (2 ml) and the flask washed with CH_2Cl_2 (0.5 ml). After stirring (0.5 h) triethylamine (1.50 ml, 5 equiv.) was added and the mixture allowed to reach room temperature, poured into ice, diluted with ether and the organic layer washed with dilute hydrochloric acid (25 ml, 0.5 mol dm^{-3}) and then water. The ether layer was separated, dried ($MgSO_4$) and concentrated to give an oil (870 mg). Chromatography on silica (50 g) eluting with benzene–ether (22:3) gave the *methyl ester* of **13a** as an oil (765 mg, 85%) (Found: C, 63.9; H, 6.1; S, 7.5. $C_{23}H_{26}O_6S$ requires C, 64.2; H, 6.1; S, 7.4%); ν_{max}(film)/cm^{-1} 1730 and 1680; δ_H(300 MHz) 1.30 (2H, m), 1.48 (2H, m), 1.70 (1H, m), 2.09 (1H, m), 2.21 (2H, m), 3.65 (3H, s, CO_2Me), 3.88 (3H, s, OMe), 4.84 (1H, t, *J* 7.5, methine-H), 6.29 (1H, d, *J* 15.0), 6.92 (3H, m), 7.58 (3H, m, SO_2Ph), 7.75 (1H, d, *J* 9.0, Ar-H), 7.87 (2H, m, SO_2Ph) and 10.02 (1H, s, CHO); *m/z* 430 (M^+), 229, 213, 189, 161, 148, 125, 121, 91 and 77 (18.5, 58.4, 85.8, 69.0, 100.0, 51.5, 41.0, 46.5, 39.1 and 95.9%). The foregoing methyl ester (510 mg, 1.19 mmol), potassium carbonate (330 mg, 2.4 mmol), methanol (12.5 ml) and water (6.3 ml) were stirred at room temperature (20 h). Hydrochloric acid (2 mol dm^{-3}) was added to reach pH 1 and the precipitated acid extracted into CH_2Cl_2. The organic layer was separated, dried ($MgSO_4$) and concentrated to give the crude acid. Chromatography on silica (35 g) eluting with benzene–ether–acetic acid (63:35:2) gave 2-(2-*formyl*-5-*methoxyphenyl*)-8-*phenylsulfonyloct*-7-*enoic acid* **13a** as an oil (426 mg, 86%) (Found: M^+, 416.1297. $C_{22}H_{24}O_6S$ requires M^+, 416.1294); ν_{max}(film)/cm^{-1} 3250, 1710 and 1685; δ_H(300 MHz) 1.40 (4H, m), 1.73 (1H, m), 2.20 (3H, m), 3.83 (3H, s, OMe), 4.73 (1H, t, *J* 7.0, methine-H), 6.28 (1H, d, *J* 16.0), 6.93 (3H, m), 7.57 (3H, m, SO_2Ph), 7.75 (1H, d, *J* 8.0, Ar-H), 7.86 (2H, m, SO_2Ph) and 9.95 (1H, s, CHO); the CO_2H signal was not recorded; *m/z* 416 (M^+), 306, 229, 213, 189, 161, 148, 121, 91 and 77 (5.0, 40.4, 72.4, 100.0, 45.6, 74.3, 27.9, 35.7, 39.4 and 61.8%).

Preparation of the aldehydo acid 13b from 12b

This proceeded as described above for **13a** *via* the hydroxymethyl ester and the methyl ester of **13b**. The hydroxymethyl ester was obtained in 97% crude yield and was directly oxidised to the *aldehydo ester* (oil, 83% yield) (Found: C, 65.0; H, 6.7; S, 7.1. $C_{25}H_{30}O_6S$ requires C, 65.2; H, 6.6; S, 7.0%); ν_{max}(film)/cm^{-1} 1725 and 1680; δ_H(300 MHz) 1.01 (6H, s, 2 × Me), 1.20 (2H, m), 1.40 (2H, m), 1.68 (1H, m), 2.04 (1H, m), 3.65 (3H, s, CO_2Me), 3.88 (3H, s, OMe), 4.84 (1H, t, *J* 6.0, methine-H), 6.15 (1H, d, *J* 15.5, olefinic-H), 6.90 (3H, m), 7.65 (3H, m, SO_2Ph), 7.74 (1H, d, *J* 4.5, Ar-H), 7.85 (2H, m, SO_2Ph) and 10.03 (1H, s, CHO); *m/z* 458 (M^+), 257, 241, 189, 161, 148, 125, 121, 77 and 41 (12.9, 56.6, 36.0, 82.9, 100.0, 43.6, 59.0, 36.4, 58.8 and 39.2%). Swern oxidation gave 2-(2-*formyl*-5-*methoxyphenyl*)-6,6-*dimethyl*-8-*phenylsulfonyloct*-7-*enoic acid* **13b** as an oil (92%) (Found: M^+, 444.1586. $C_{24}H_{28}O_6S$ requires M^+, 444.1606); ν_{max}(film)/cm^{-1} 3350, 1730 and 1690; δ_H(300 MHz) 0.99 (6H, s, 2 × Me), 1.20 (2H, m), 1.41 (2H, m), 1.69 (1H, m), 2.10 (1H, m), 3.87 (3H, s, OMe), 4.73 (1H, t, *J* 7.0, methine-H), 6.13 (1H, d, *J* 15.5, olefinic-H), 6.87 (1H, d, *J* 15.5, olefinic-H), 6.93 (2H, m), 7.56 (3H, m), 7.75 (1H, d, *J* 8.0, Ar-H), 7.83 (2H, m), 9.96 (1H, s, CHO); the CO_2H signal was not recorded; *m/z* 444 (M^+), 334, 257, 241, 189, 171, 161, 125, 77 and 41 (6.0, 47.6, 72.5, 78.9, 78.2, 72.8, 100.0, 64.0, 77.8 and 56.6%).

Attempted base catalysed ring opening of 12c

The vinyl sulfone **12c** (200 mg, 0.517 mmol), potassium carbon-

ate (143 mg, 1.04 mmol), methanol (5 ml) and water (2.6 ml) were stirred at 20 °C (15 h). The product was cooled to 0 °C and acidified with hydrochloric acid (2 M). The product was extracted into ice cold ether and treated with ethereal diazomethane at 0 °C. The evaporated product was chromatographed on silica to give initially one diastereoisomer of **14** (21 mg, 10%) as a white solid; δ_H(400 MHz) 1.66 (1H, dt, *J* 14.0 and 9.5), 1.88 (2H, m), 2.06 (1H, m), 2.19 (1H, m), 2.50 (1H, dt, *J* 13.5 and 6.0), 3.10 (1H, dd, *J* 14.0 and 1.0, C*H*$_2$SO$_2$Ph), 3.22 (1H, q, *J* 10.0, C*H*CH$_2$SO$_2$Ph), 3.66 (1H, dd, *J* 14.0 and 10, C*H*$_2$SO$_2$Ph), 3.9 (3H, s), 5.10 (1H, d, *J* 14.0, benzylic-H), 5.40 (1H, d, *J* 14, benzylic-H), 6.83 (1H, m), 7.1 (2H, m), 7.57 (2H, m), 7.63 (1H, m) and 7.90 (2H, m); *m/z* 386, 245, 217, 216, 199, 177, 159 (7, 66, 30, 60, 73, 100 and 31%).

Continued elution of the column gave a second diastereoisomer of **14** (73 mg, 34%); δ_H(400 MHz) 1.84 (2H, m), 2.08 (3H, m), 2.37 (1H, m), 2.66 (1H, dd, *J* 14.5 and 2.5, C*H*$_2$SO$_2$Ph), 2.84 (1H, dd, *J* 14.5 and 10.5, C*H*$_2$SO$_2$Ph), 2.94 (1H, m, C*H*CH$_2$SO$_2$Ph), 3.83 (3H, s), 5.01 (2H, AB system, *J* 14.0, benzylic-H), 6.79 (1H, m), 6.85 (1H, m), 7.08 (1H, m), 7.55 (2H, m), 7.65 (1H, m), 7.75 (2H, m).

Continued elution of the column gave the desired hydroxy ester (52 mg, 24%); δ_H 1.77–2.29 (m, 6H), 3.64 (3H, s), 3.79 (3H, s), 3.97 (1H, t, *J* 7), 4.66 (2H, s, benzylic-H), 6.30 (1H, d, *J* 15, olefinic-H), 6.77 (1H, d, *J* 9.0, Ar-H), 6.86 (1H, s, Ar-H), 6.91 (1H, m, olefinic-H), 7.25 (1H, m, Ar-H), 7.55 (3H, m, Ar-H) and 7.86 (2H, m, Ar-H). This compound was not further characterised.

Intramolecular Diels–Alder addition of 2e

The aldehydo acid **13a** (114 mg, 0.27 mmol) was dissolved in freshly distilled acetic anhydride (5.5 ml) and heated at reflux (0.5 h) under argon. The solvent was removed under reduced pressure with heating, and chromatography on silica (32 g) eluting with benzene–ether (23:2) gave initially the exo-6-*methoxy*-12-*oxo*-10-*phenylsulfonyl*-2,3,4,9,10,10a-*hexahydro*-1H-9,4a-(*epoxymethano*)*phenanthrene* **4e** (74 mg, 68%), mp 231.5–233.0 °C (methanol–dichloromethane) (Found: C, 66.2; H, 5.6; S, 8.3. $C_{22}H_{22}O_5S$ requires C, 66.3; H, 5.5; S, 8.0%); ν_{max}(film)/cm^{-1} 1745; δ_H(400 MHz) 1.14 (1H, qd, *J* 13.0 and 2.5), 1.24 (1H, m), 1.68 (2H, m), 1.87 (3H, m), 2.14 (1H, ddd, *J* 12.5, 6.0 and 4.0, *endo*-methine), 2.57 (1H, br d, *J* 11.0), 3.62 (1H, dd, *J* 3.0 and 6.0, *exo*-methine), 3.84 (3H, s, OMe), 5.58 (1H, d, *J* 3.0, bridgehead methine), 6.85 (2H, m, Ar-H), 7.31 (1H, d, *J* 8.0, Ar-H), 7.60 (2H, m, SO$_2$Ph), 7.70 (1H, m, SO$_2$Ph) and 7.84 (2H, m, SO$_2$Ph); *m/z* 398 (M$^+$), 214, 213, 212, 198, 184, 171, 141, 128 and 77 (7.8, 17.3, 100.0, 10.0, 5.0, 5.0, 31.4, 7.3, 6.8 and 6.5%).

Further elution of the column gave the endo-*chain adduct* **3e** (17.5 mg, 16%), mp 116.0–118 °C (dichloromethane–methanol) (Found: M$^+$, 398.1200. $C_{22}H_{22}O_5S$ requires *M*$^+$, 398.1188); ν_{max}(film)/cm^{-1} 1760; δ_H(400 MHz) 0.78 (1H, qd, *J* 13.0 and 3.0), 1.33 (1H, m), 1.57 (1H, m), 1.73 (2H, m), 1.87 (1H, m), 2.05 (1H, td, *J* 14.0 and 5.0), 2.33 (1H, ddd, *J* 12.0, 5.5 and 3.5, *exo*-methine), 2.47 (1H, br d, *J* 14.0), 2.94 (1H, dd, *J* 5.5 and 1.0, *endo*-methine), 3.82 (3H, s, OMe), 5.81 (1H, d, *J* 0.5, bridgehead methine), 6.78 (1H, dd, *J* 8.0 and 2.5, Ar-H), 6.95 (1H, d, *J* 2.5, Ar-H), 7.22 (1H, d, *J* 8.0, Ar-H), 7.62 (2H, m, SO$_2$Ph), 7.72 (1H, m, SO$_2$Ph) and 7.99 (2H, m, SO$_2$Ph); *m/z* 398 (M$^+$), 229, 214, 213, 212, 201, 171, 92, 91 and 77 (6.8, 38.7, 30.9, 100.0, 14.2, 31.2, 36.8, 51.9, 66.7 and 24.4%).

Intramolecular Diels–Alder addition of 2f

In the same way as described above, **2f**, generated by acetic anhydride dehydration of **13b**, gave endo- *and* exo-1,1-*dimethyl*-6-*methoxy*-12-*oxo*-10-*phenylsulfonyl*-2,3,4,9,10,10a-*hexahydro*-9,4a-(*epoxymethano*)*phenanthrene* **3f** and **4f**. The *exo*-chain adduct **4f** (32.3 mg, 60%) mp 158.5–160.0 °C (EtOH) (Found: C, 67.5; H, 6.3; S, 7.5. $C_{24}H_{26}O_5S$ requires C, 67.6; H, 6.1; S, 7.5%); ν_{max}(film)/cm^{-1} 1750; δ_H(300 MHz) 0.73 (3H, s, Me), 0.88 (3H, s, Me), 1.28 (1H, m), 1.53 (1H, m), 1.75 (1H, m), 1.84 (1H, dd, *J* 4.5 and 13.0), 2.05 (2H, m), 2.56 (1H, d, *J* 13.0), 3.83 (3H, s, OMe), 4.12 (1H, t, *J* 4.5, *exo*-methine), 5.74 (1H, d, *J* 4.0, bridgehead methine), 6.78 (1H, d, *J* 2.0, Ar-H), 6.86 (1H, dd, *J* 2.0 and 8.5, Ar-H), 7.29 (1H, d, *J* 8.5, Ar-H), 7.52 (3H, m, SO$_2$Ph) and 7.65 (2H, m, SO$_2$Ph); *m/z* 426 (M$^+$), 242, 241, 185, 172, 171, 128, 77, 55 and 41 (20.8, 34.8, 96.4, 17.8, 29.7, 100.0, 24.2, 38.6, 20.9 and 17.9%).

The endo-*chain adduct* **3f** (24%) mp 197.0–197.5 °C (EtOH) (Found: C, 67.7; H, 6.3; S, 7.6%); ν_{max}(film)/cm^{-1} 1755; δ_H(300 MHz) 0.14 (3H, s, Me), 1.03 (3H, s, Me), 1.33 (2H, m), 1.85 (3H, m), 2.32 (1H, d, *J* 4.5, *exo*-methine), 2.48 (1H, d, *J* 12.0), 3.43 (1H, d, *J* 4.5, *endo*-methine), 3.80 (3H, s, OMe), 5.64 (1H, s, bridgehead methine), 6.76 (1H, dd, *J* 2.0 and 8.5, Ar-H), 6.96 (1H, d, *J* 2.0, Ar-H), 7.16 (1H, d, *J* 8.0, Ar-H), 7.68 (3H, m, SO$_2$Ph) and 8.07 (2H, m, SO$_2$Ph); *m/z* 426 (M$^+$), 257, 242, 241, 229, 172, 171, 77, 69 and 41 (5.8, 72.6, 58.7, 100.0, 48.4, 47.9, 97.9, 67.1, 54.4 and 37.7%).

Desulfurisation of adduct 4e

To a solution of the sulfone (50 mg, 0.13 mmol) was added anhydrous disodium orthophosphate (90 mg, 4 equiv., 0.5 mmol), dry methanol (3 ml) and dry distilled THF (3.0 ml). The flask was cooled to 0–5 °C (ice–water), pulverised 5% sodium–mercury amalgam (130 mg) was added, and the reaction stirred under argon (18 h). The product was poured into water, acidified to pH 1 with hydrochloric acid (2 mol dm^{-3}), extracted into ether, dried (MgSO$_4$) and concentrated to give the crude product (61 mg). Chromatography on silica (22 g) eluting with benzene–ether–acetic acid (46:3:1) gave 6-*methoxy*-1,2,3,4,4a,10a-*hexahydrophenanthrene*-4-*carboxylic acid* **32** (27 mg, 83%) (Found: C, 74.2; H, 7.1. $C_{16}H_{18}O_3$ requires C, 74.4; H, 7.0%) mp 195.0–197.5 °C (dichloromethane–light petroleum); ν_{max}(Nujol)/cm^{-1} 2860 and 1685; δ_H(400 MHz) 1.47 (2H, m), 1.68 (1H, td, *J* 13.0 and 3.0), 1.83 (1H, m), 1.90 (2H, br d, *J* 13.0), 2.16 (1H, qd, *J* 13.0 and 3.5), 2.53 (1H, dq, *J* 13.0 and 3.0, methine-H), 2.84 (1H, br d, *J* 13.0), 3.88 (3H, s, OMe), 5.80 (1H, dd, *J* 2.5 and 9.5, olefinic-H), 6.40 (1H, dd, *J* 3.0 and 9.5, olefinic-H), 6.82 (1H, dd, *J* 2.5 and 8.5, Ar-H) and 7.05 (2H, m, Ar-H); the CO$_2$H signal was not recorded; *m/z* 258 (M$^+$), 214, 213, 212, 171, 149, 143, 141, 125 and 113 (31.5, 23.3, 100.0, 30.8, 52.4, 18.7, 35.9, 16.3, 31.3 and 15.0%).

Desulfurisation of adduct 3e

To a solution of the sulfone **3e** (25 mg, 0.063 mmol) was added anhydrous disodium orthophosphate (45 mg, 4 equiv., 0.03 mmol), dry methanol (1.5 ml) and dry distilled THF (1.5 ml). The flask was cooled to 0–5 °C (ice–water), pulverised 5% sodium–amalgam (65 mg) was added, and the reaction stirred under argon (2 h) after being allowed to rise to room temperature. The product was poured into water, acidified to pH 1 with hydrochloric acid (2 mol dm^{-3}), extracted into ether, dried (MgSO$_4$) and concentrated to give the crude product. Chromatography on silica (20 g) eluting with benzene–ether–acetic acid (44:5:1) gave the (4aS,10aS)-1,1-*dimethyl*-6-*methoxy*-1,2,3,4,4a,10a-*hexahydrophenanthrene*-4a-*carboxylic acid* **35** (4.8 mg, 30%) (Found: M$^+$, 258.1252. $C_{16}H_{18}O_3$ requires *M*$^+$, 258.1256); ν_{max}(film)/cm^{-1} 2920 and 1690; δ_H(400 MHz) 1.25 (2H, m), 1.40 (1H, m), 1.55 (3H, m), 1.86 (1H, m), 2.23 (1H, br s), 2.95 (1H, br s, *exo*-methine), 3.80 (3H, s, OMe), 5.83 (1H, dd, *J* 10.0 and 5.0, olefinic-H), 6.37 (1H, d, *J* 10.0, olefinic-H), 6.75 (1H, dd, *J* 8.0 and 2.5, Ar-H), 6.89 (1H, d, *J* 2.0, Ar-H) and 7.02 (1H, d, *J* 8.0, Ar-H); the CO$_2$H signal was not recorded; *m/z* 258 (M$^+$), 214, 213, 212, 184, 172, 171, 141, 128 and 115 (30.0, 23.7, 100.0, 36.1, 11.5, 10.4, 54.0, 13.1, 17.4 and 14.6%).

Further elution of the column gave the (4aS,10aS)-1,1-*dimethyl*-6-*methoxy*-10-*phenylsulfonyl*-1,2,3,4,4a,9,10,10a-*octahydrophenanthrene*-4a-*carboxylic acid* **34** (14.3 mg, 57%) (Found: M$^+$, 400.1335. $C_{22}H_{24}O_5S$ requires *M*$^+$, 400.1344); ν_{max}(film)/cm^{-1} 3050 and 1700; δ_H(400 MHz) 1.18 (1H, m), 1.32

(2H, m), 1.56 (1H, m), 1.67 (1H, m), 1.82 (1H, td, *J* 13.5 and 3.5), 2.23 (1H, m), 2.62 (1H, br d, *J* 14.0), 2.83 (1H, m, *exo*-methine), 2.86 (1H, dd, *J* 16.5 and 6.0, benzylic-H), 3.31 (1H, dd, *J* 16.5 and 13.0, benzylic-H), 3.67 (1H, ddd, *J* 13.0, 6.0 and 2.5, C*H*SO_2Ph), 3.80 (3H, s, OMe), 6.80 (1H, dd, *J* 8.5 and 2.5, Ar-H), 6.99 (1H, d, *J* 2.5, Ar-H), 7.05 (1H, d, *J* 8.5, Ar-H), 7.62 (3H, m, SO_2Ph) and 7.92 (2H, m, SO_2Ph); *m/z* 400 (M^+), 259, 258, 214, 213, 212, 172, 171, 78 and 77 (2.0, 19.8, 59.5, 26.1, 100.0, 23.9, 9.9, 35.7, 22.9 and 18.5%).

Desulfurisation of the adduct 4f

To a solution of the sulfone **4f** (23 mg, 0.054 mmol) was added anhydrous disodium orthophosphate (42 mg, 4 equiv., 0.22 mmol), dry methanol (1.5 ml) and dry distilled THF (1.5 ml). The flask was cooled to 0–5 °C (ice–water), pulverised 5% sodium–amalgam (60 mg) was added, and the reaction stirred under argon (18 h). The product was poured into water, acidified to pH 1 with hydrochloric acid (2 mol dm^{-3}), extracted into ether, dried ($MgSO_4$) and concentrated to give the crude product (23 mg). Chromatography on silica (35 g) eluting with benzene–ether–acetic acid (93:5:2) gave the (4aS,10aR)-1,1-*dimethyl*-6-*methoxy*-1,2,3,4,4a,10a-*hexahydrophenanthrene*-4a-*carboxylic acid* **33** (12.8 mg, 83%) mp 208–210 °C (dichloromethane–ethanol) (Found: C, 75.5; H, 7.8. $C_{18}H_{22}O_3$ requires C, 75.7; H, 7.7%); ν_{max}(Nujol)/cm^{-1} 2880 and 1685; δ_H(300 MHz) 0.96 (3H, s, Me), 1.04 (3H, s, Me), 1.40 (3H, m), 1.80 (2H, m), 2.56 (1H, t, *J* 2.0), 2.97 (1H, d, *J* 12.5), 3.79 (3H, s, OMe), 6.11 (1H, dd, *J* 2.5 and 9.5, olefinic-H), 6.60 (1H, dd, *J* 3.5 and 9.6, olefinic-H), 6.74 (1H, dd, *J* 2.4 and 8.3, Ar-H), 6.91 (1H, d, *J* 2.2, Ar-H) and 7.04 (1H, d, *J* 8.3, Ar-H); the CO_2H signal was not recorded; *m/z* 286 (M^+), 242, 241, 204, 202, 185, 172, 171, 128 and 115 (33.7, 30.4, 38.1, 40.5, 18.7, 15.0, 24.2, 100.0, 17.9 and 13.9%).

Wadsworth–Horner–Emmons reaction of aldehyde 11a

To a stirred solution of sodium hydride (108 mg, 2.69 mmol of a 60% dispersion in mineral oil) in dry 1,2-dimethoxyethane (DME) (3.0 ml) was added dropwise trimethyl phosphonoacetate (533 mg, 2.9 mmol) in DME (2.5 ml) at room temperature. The aldehyde **11a** (640 mg, 2.44 mmol) in DME (2.5 ml) was added dropwise and the reaction stirred (5 min). The reaction was quenched with water, diluted with ether and the organic layer was washed with saturated brine. The ether layer was separated, dried ($MgSO_4$) and concentrated to give an oil. Chromatography on silica (60 g) eluting with benzene–ether (4:1) gave initially a mixture of *alcohols* produced by intramolecular aldolisation (Claisen reaction) of the starting material (13 mg, 21%) (Found: C, 68.7; H, 7.15. $C_{15}H_{18}O_4$ requires C, 68.7; H, 6.9%); ν_{max}(film)/cm^{-1} 3460 and 1720; δ_H(300 MHz) 1.08–1.65 (4H, m), 1.89 (1H, m), 2.19 (1H, m), 2.31 (2H, m), 2.47 (1H, m), 3.84 (3H, s, OMe), 4.21 (1H, m, C*H*OH), 5.24 (1H, d, *J* 14.0, benzylic-H), 5.53 (1H, d, *J* 14.0, benzylic-H) and 6.83 (1H, dd, *J* 2.5 and 8.0, Ar-H) and 7.10 (2H, m, Ar-H); *m/z* 262 (M^+), 199, 191, 163, 159, 147, 145, 121, 91 and 32 (100.0, 48.7, 38.9, 32.7, 23.9, 32.0, 61.2, 23.7, 24.4 and 32.5%).

Further elution of the column gave the *methyl* 7-(6-*methoxy*-3-*oxochroman*-4-*yl*)*hept*-2-*enoate* **28** (489 mg, 63%) (Found: M^+, 318.1476. $C_{18}H_{22}O_5$ requires M^+, 318.1467); ν_{max}(film)/cm^{-1} 1720; δ_H(300 MHz) 1.53 (4H, br s), 1.85 (1H, m), 1.97 (1H, m), 2.22 (2H, d, *J* 5), 3.55 (1H, t, *J* 7.0, methine-H), 3.72 (3H, s, CO_2Me), 3.82 (3H, s, OMe), 5.20 (1H, d, *J* 14, benzylic-H), 5.38 (1H, d, *J* 14.0, benzylic-H), 5.81 (1H, d, *J* 15.5, olefinic-H), 6.71 (1H, d, *J* 2.0, Ar-H), 6.82 (1H, dd, *J* 2.0 and 8.5, Ar-H), 6.94 (1H, dt, *J* 15.5 and 7.0, olefinic-H) and 7.13 (1H, d, *J* 8.5, Ar-H); *m/z* 318 (M^+), 258, 213, 177, 149, 57, 55, 43, 41 and 40 (18.7, 53.3, 48.5, 100.0, 79.7, 69.9, 58.9, 68.7, 62.0 and 67.9%).

Preparation of the alcohol 29

The ester **28** (470 mg, 1.48 mmol), potassium carbonate (588 mg, 4.3 mmol), methanol (8.8 ml) and water (2.8 ml) were heated at reflux (1.5 h). The mixture was cooled to 0–5 °C (ice–water) and transferred to a separating funnel where ice cold dilute hydrochloric acid (2 mol dm^{-3}) was added. The precipitated *acid* was extracted into ether (0 °C) and immediately treated with diazomethane. Evaporation of the solvent left an oil which was dissolved in ether, dried ($MgSO_4$) and concentrated to give the crude *dimethyl* 8-(2-*hydroxymethyl*-5-*methoxyphenyl*)*non*-2-*enedioate* **29** (497 mg, 96%) (Found: M^+, 350.1726. $C_{19}H_{26}O_6$ requires M^+, 350.1729); ν_{max}(film)/cm^{-1} 3470 and 1725; δ_H(300 MHz, C_6D_6) 1.11 (3H, m), 1.31 (1H, m), 1.66 (3H, m) 2.02 (1H, m), 3.19 (3H, s, CO_2Me), 3.31 (3H, s, CO_2Me), 3.40 (3H, s, OMe), 3.98 (1H, t, *J* 7.5, methine-H), 4.53 (1H, d, *J* 12.5, benzylic-H), 4.62 (1H, d, *J* 12.5, benzylic-H), 5.78 (1H, d, *J* 15.5, olefinic-H), 5.60 (1H, dd, *J* 2.5 and 8.5, Ar-H), 6.94 (1H, td *J* 7.0 and 15.5, olefinic-H), 7.07 (1H, d, *J* 8.5, Ar-H) and 7.23 (1H, apparent s, Ar-H); the OH signal was not recorded; *m/z* 350 (M^+), 258, 213, 177, 161, 159, 149, 137, 121 and 91 (3.8, 33.7, 44.4, 65.6, 44.1, 34.1, 31.1, 100.0, 47.8 and 37.8%).

Swern oxidation of 29

To a stirred solution of DMSO (342 mg, 4.4 mmol) in dry dichloromethane (4 ml) was added oxalyl chloride (278 mg, 2.2 mmol) in CH_2Cl_2 (4 ml) at −78 °C with stirring under argon. The solution was stirred (4 min) then the alcohol **29** added dropwise (510 mg, 1.46 mmol) in CH_2Cl_2 (6 ml) and the flask washed with CH_2Cl_2 (1.5 ml). After stirring (0.75 h), triethylamine (1.0 ml) was added and the mixture stirred at −78 °C (10 min) then allowed to reach room temperature, poured onto ice and diluted with ether. The organic layer was washed with dilute HCl and then water, dried ($MgSO_4$) and concentrated to give an oil. Chromatography on silica (35 g) eluting with benzene–ether (9:1) gave *dimethyl* 8-(2-*formyl*-5-*methoxyphenyl*)*non*-2-*enedioate* **30** as an oil (448 mg, 88%) (Found: C, 65.4; H, 6.6. $C_{19}H_{24}O_6$ requires C, 65.5; H, 6.9%); ν_{max}(film)/cm^{-1} 1715 and 1680; δ_H(300 MHz) 1.33 (2H, m), 1.48 (2H, m), 1.74 (1H, m), 2.15 (3H, m), 3.66 (3H, s, CO_2Me), 3.72 (3H, s, CO_2Me), 3.88 (3H, s, OMe), 4.85 (1H, t, *J* 7.5, methine-H), 5.79 (1H, d, *J* 15.5, olefinic-H), 6.93 (3H, m, olefinic-H and 2 × Ar-H), 7.77 (1H, d, *J* 8.0, Ar-H) and 10.05 (1H, s, CHO); *m/z* 348 (M^+), 298, 229, 213, 211, 190, 189, 162, 161 and 148 (8.4, 32.5, 32.9, 64.2, 32.2, 37.4, 64.7, 30.2, 100.0 and 47.5%).

Selective hydrolysis of 30

Compound **30** (38 mg, 0.11 mmol) was dissolved in methanol (1.1 ml), containing potassium carbonate (60 mg, 0.44 mmol) and water (0.3 ml) and stirred at room temperature (17 h). Hydrochloric acid (2 mol dm^{-3}) was added to reach pH 1 and the precipitated acid extracted into CH_2Cl_2. The organic layer was separated, dried ($MgSO_4$) and concentrated to give the crude acid. Chromatography on silica (32 g) eluting with benzene–ether–acetic acid (45:5:1) gave 1-*methyl hydrogen* 8-(2-*formyl*-5-*methoxyphenyl*)*non*-2-*enedioate* **31** as an oil (33 mg, 90%) (Found: M^+, 334.1478. $C_{18}H_{22}O_6$ requires M^+, 334.1421); ν_{max}(film)/cm^{-1} 3100 and 1740–1650; δ_H(300 MHz) 1.40 (4H, m), 1.75 (1H, m), 2.17 (3H, m), 3.72 (3H, s, CO_2Me), 3.89 (3H, s, OMe), 4.76 (1H, t, *J* 7.0, methine-H), 5.78 (1H, d, *J* 15.5, olefinic-H), 6.96 (3H, m, olefinic-H and 2 × Ar-H), 7.76 (1H, d, *J* 8.5, Ar-H) and 9.99 (1H, s, CHO); the CO_2H signal was not recorded; *m/z* 334 (M^+), 214, 213, 212, 211, 189, 171, 162, 161 and 148 (0.5, 26.4, 100.0, 35.8, 26.5, 44.2, 27.9, 26.4, 82.8 and 32.8%).

Intramolecular Diels–Alder addition of 2g

The aldehydo acid **31** (25 mg, 0.075 mmol) was dissolved in dry distilled acetic anhydride and heated at reflux (1 h). The solvent was removed under reduced pressure with heating, and chromatography on silica (45 g) eluting with benzene–ether (23:2) gave initially the exo-*methyl* 6-*methoxy*-12-*oxo*-2,3,4,9,10,10a-

hexahydro-9,4a-(*epoxymethano*)*phenanthrene*-10-*carboxylate* **4g** (17 mg, 72%) (Found: M^+, 316.1426. $C_{18}H_{20}O_5$ requires M^+, 316.1461); ν_{max}(film)/cm^{-1} 1740; δ_H(300 MHz) 1.28 (2H, m), 1.90 (5H, m), 2.13 (1H, br d, *J* 12.5), 2.57 (1H, br d, *J* 12.5), 3.00 (1H, dd, *J* 3.5 and 5.5), 3.62 (3H, s, CO_2Me), 3.81 (3H, s, OMe), 5.69 (1H, d, *J* 3.5, bridgehead methine), 6.76 (1H, dd, *J* 2.0 and 8.0), 6.81 (1H, br s) and 7.21 (1H, d, *J* 8.0); *m/z* 316 (M^+), 272, 214, 213, 212, 171, 161, 141, 128 and 125 (29.6, 38.6, 32.8, 100.0, 43.1, 46.8, 16.1, 17.6, 20.0 and 17.7%).

Further elution of the column gave the endo-*chain adduct* **3g** (5.0 mg, 21%) (Found: M^+, 316.1469); ν_{max}(film)/cm^{-1} 1745; δ_H(300 MHz) 0.80 (1H, m), 1.27 (1H, m), 1.43 (1H, m), 1.76 (2H, m), 1.89 (1H, m), 2.15 (1H, td, *J* 13.0 and 4.5), 2.31 (1H, d, *J* 5.0), 2.49 (2H, m), 3.81 (3H, s, CO_2Me), 3.84 (3H, s, OMe), 5.79 (1H, s, bridgehead methine), 6.79 (1H, d, *J* 2.0, Ar-H), 7.00 (1H, s, Ar-H), 7.25 (1H, s, Ar-H); *m/z* 316 (M^+), 272, 214, 213, 212, 184, 171, 141, 128 and 115 (12.4, 50.0, 40.5, 100.0, 52.3, 19.9, 56.4, 20.6, 25.3 and 23.0%).

Synthesis of the ethyl ester 15

Ethyl *o*-formylphenylacetate (300 mg, 1.5 mmol), ethylene glycol (2.42 g, 37 mmol, 25 equiv.), trimethyl orthoformate (795 mg, 7.5 mmol, 5 equiv.) and a catalytic amount of toluene-*p*-sulfonic acid (5 mg) were refluxed in dry benzene (15 ml) using a Dean–Stark trap for 2 h. The reaction mixture was poured into saturated aqueous hydrogen sodium carbonate and extracted with ether (3 × 15 ml). The extracts were washed with brine and then water, dried ($MgSO_4$) and evaporated under reduced pressure to give a pale yellow oil. Chromatography on silica (60 g) eluting with light petroleum–ether (7:3) gave the *ethyl* 2-[2-(1,3-*dioxolan*-2-*yl*)*phenylacetate*] **15** as a pale yellow oil (220 mg, 63%); ν_{max}(film)/cm^{-1} 1733; δ_H(300 MHz) 1.22 (3H, t, *J* 7, CH_2CH_3), 3.78 (2H, s, benzylic-H), 3.97–4.17 (6H, m, acetal-H and CH_2CH_3), 5.94 (1H, s, acetal-H) and 7.23–7.53 (4H, m, Ar-H); *m/z* 236 (M^+), 235, 191, 149, 119, 91 and 73 (1, 5, 18, 100, 23, 52 and 20%).

Synthesis of the alkylated ester 17

Potassium bis(trimethylsilyl)amide in THF (0.5 mol dm^{-3}, 0.92 ml, 1.1 equiv.) was added to a stirred solution of the acetal **15** (100 mg, 0.42 mmol) in dry THF (5 ml) at room temperature under argon. Hexamethylphosphoramide (HMPA) (0.067 ml) and 5-iodopent-1-ene (90 mg, 0.46 mmol) were added and the mixture stirred (20 h). The reaction mixture was quenched with water and extracted with ether. The ethereal extracts were washed with saturated aqueous ammonium chloride and then water, dried ($MgSO_4$) and evaporated under reduced pressure to give a yellow oil. Chromatography on silica (25 g) eluting with light petroleum–ether (3:1) gave the *ethyl* 2-[2-(1,3-*dioxolan*-2-*yl*)*phenyl*]*hept*-6-*enoate* **17** (69 mg, 54%) (Found: M^+, 304.1662. $C_{18}H_{24}O_4$ requires M^+, 304.1674); ν_{max}(film)/cm^{-1} 1725 (s); δ_H(300 MHz) 1.20 (3H, t, *J* 7), 1.28–2.20 (6H, m, side chain), 3.96–4.18 (7H, m, ethylene acetal, CH_2CH_3 and benzylic-H), 4.97 (2H, m, methylene-H), 5.98 (1H, m, methine-H), 6.10 (1H, s, acetal-H) and 7.20–7.6 (4H, m, Ar-H); *m/z* 304 (M^+), 303, 275, 169, 149, 115, 91, 73 and 45 (1, 8, 4, 31, 30, 29, 49, 21 and 37%).

Synthesis of the alkylated ester 16

Potassium bis(trimethylsilyl)amide in THF (0.5 mol dm^{-3}, 42 ml, 1.1 equiv.) was added to a stirred solution of the acetal **15** (3.1 g, 15 mmol) in dry THF (120 ml) at room temperature under argon. HMPA (4 ml) and 6-iodohex-1-ene (3.6 g, 17 mmol) were added and the mixture stirred (20 h). The reaction mixture was quenched with water, extracted with ether, the ethereal extracts washed with saturated aqueous ammonium chloride and then water, dried ($MgSO_4$) and evaporated under reduced pressure to give a yellow oil. Chromatography on silica (125 g) eluting with light petroleum–ether (3:1) gave the *ethyl* 2-[2-(1,3-*dioxolan*-2-*yl*)*phenyl*]*oct*-7-*enoate* **16** (2.86 g, 60%) (Found: C, 71.5; H, 7.9. $C_{19}H_{26}O_4$ requires C, 71.6; H, 8.2%); ν_{max}(film)/cm^{-1} 1731; δ_H(300 MHz) 1.18 (3H, t, *J* 7), 1.25–2.10 (8H, m, side chain), 4.0–4.18 (7H, m, ethylene acetal, CH_2CH_3 and benzylic-H), 4.93 (2H, m, methylene-H), 5.75 (1H, m, methine-H), 6.07 (1H, s, acetal-H) and 7.22–7.58 (4H, m, Ar-H); *m/z* 318 (M^+), 317, 273, 175, 149, 91 and 73 (1, 2, 4, 6, 100, 19 and 17%).

Hydrolysis of the ethyl ester 17

The ethyl ester (50 mg, 0.16 mmol), methanol (2 ml), potassium carbonate (45 mg, 0.32 mmol, 2 equiv.) and water (1 ml) were refluxed under argon (2 h). Most of the methanol was removed on a rotary evaporator and the residue acidified to pH 1 using 2 M hydrochloric acid. The precipitated acid was extracted into dichloromethane, the organic layer washed with saturated aqueous sodium hydrogen carbonate and the aqueous layer carefully acidified using 2 M hydrochloric acid. The acid was extracted from the aqueous layer with ether, the ethereal extracts dried ($MgSO_4$) and evaporated under reduced pressure to give the 2-(2-*formylphenyl*)*hept*-6-*enoic acid* **19** as a colourless oil (25 mg, 58%); ν_{max}(film)/cm^{-1} 3690–2290 (OHbr) and 1713; δ_H(300 MHz) 1.25–2.16 (6H, m, side chain), 4.03–4.23 (5H, m, acetal and benzylic-H), 4.94 (2H, m, methylene-H), 5.74 (1H, m, methine-H), 6.02 (1H, s, acetal-H) and 7.26–7.56 (4H, m, Ar-H); *m/z* 276 (M^+), 275, 149, 91 and 73 (3, 5, 100, 31 and 20%).

Preparation of 13c

A solution of the carboxylic acid **19** (50 mg, 0.8 mmol) and *Se*-phenyl benzeneselenosulfonate (53 mg, 0.8 mmol) in dry degassed benzene (2 ml) was irradiated through Pyrex using a water-cooled Hanovia UV lamp (125 W) for 10 min at room temperature. The solvent was evaporated and the residue taken up in dichloromethane (1 ml); 30% aqueous hydrogen peroxide (0.5 ml) was added with vigorous stirring at 0 °C. After continued stirring for 30 min at 0 °C the reaction mixture was allowed to warm to room temperature. The solution was poured into 5% aqueous sodium hydrogen carbonate (3 ml) and dichloromethane (3 ml) and the layers separated. The organic layer was then washed with more aqueous sodium hydrogen carbonate and the aqueous layer acidified using 2 M HCl and the acid taken up into ethyl acetate. The organic layer was washed with water before drying ($MgSO_4$) and evaporation. The residue was dissolved in THF (90 ml) and 4 M hydrochloric acid (18 ml), and was stirred overnight before extracting into ether. The extracts were dried ($MgSO_4$) and evaporated to give 2-(2-*formylphenyl*)-7-*phenylsulfonylhept*-6-*enoic acid* **13c** as an oil (51 mg, 70%); ν_{max}(film)/cm^{-1} 3758–3158 (OHbr) and 1698; δ_H(300 MHz) 1.47–2.28 [6H, m, $(CH_2)_3$ chain], 4.85 (1H, br, benzylic-H), 6.30 (1H, d, *J* 14, vinylic-H), 6.93 (1H, td, *J* 7, 14, vinylic-H), 7.39–7.87 (9H, m) and 9.00–9.60 (1H, br s, CO_2H), 10.13 (1H, s, CHO); *m/z* 372 (M^+), 275, 149, 141 and 91 (5, 20, 100, 51 and 30%).

Preparation of acid 13d

Starting with ester **16** this involved a modified sequence of the reactions used to make **13c** from **17**, but very similar conditions for the individual steps. The ethyl ester **16** gave the ethyl ester of **21** which was hydrolysed first with dilute acid and then with K_2CO_3–MeOH–H_2O to give the 2-(2-*formylphenyl*)-8-*phenylsulfonyloct*-7-*enoic acid* **13d** (37% over 3 steps) (Found: M^+, 386.1726. $C_{21}H_{22}O_5S$ requires *M*, 386.1725); ν_{max}(film)/cm^{-1} 2500–3600 (br), 2210, 1710 and 1690; δ_H(300 MHz) 1.20–2.28 (4H, m), 1.75 (1H, m), 2.18 (3H, m), 4.72 (1H, br, benzylic-H), 6.30 (1H, d, *J* 14, vinyl sulfone), 6.95 (1H, dt, *J* 14 and 7.4, vinyl sulfone), 7.4–7.68 (6H, m, Ar-H), 7.79–7.98 (3H, m, Ar-H) and 10.1 (1H, br s, CHO); the CO_2H signal was not recorded; *m/z* 386 (M^+), 362, 244, 141 and 77 (8, 21, 26, 60 and 100%).

Intramolecular Diels–Alder addition of 2d

The foregoing aldehydo acid **13d** (50 mg, 0.13 mmol) and freshly distilled acetic anhydride (1 ml) were boiled under reflux (0.5 h) under argon. The solvent was removed under reduced pressure with heating on a steam bath. Chromatography on silica (25 g) eluting with light petroleum–ethyl acetate (7:3) gave initially the exo-8-*methoxy*-11-*oxo*-4-*phenylsulfonyl*-1,2,3,3a,4,5-*hexahydro*-9b,5(*epoxymethane*)*benz*[e]*indene* **4d** (17 mg, 38%), mp 216–218 °C (ethanol) (Found: C, 67.4, H, 4.6. $C_{19}H_{18}O_4S$ requires C, 67.7, H, 5.0%); ν_{max}(Nujol)/cm^{-1} 1745; δ_H(300 MHz) 1.20 (1H, m), 1.70 (1H, m), 1.85 (1H, m), 2.25 (2H, m), 2.30 (1H, m), 2.62 (1H, m), 3.72 (1H, dd, *J* 2, 5), 5.75 (1H, d, *J* 3, bridgehead methine) and 7.29–7.85 (9H, m, Ar-H); *m/z* 354 (M^+), 169, 141, 115 and 77 (1, 100, 44, 14 and 23%).

Further elution of the column gave the endo-*chain adduct* **3d** (22 mg, 48%), mp 105–107 °C (dichloromethane–methanol) (Found: C, 67.5, H, 5.1. $C_{19}H_{18}O_4S$ requires C, 67.7, H, 5.0%); ν_{max}(Nujol)/cm^{-1} 1750; δ_H(300 MHz) 0.74 (1H, m), 1.22 (1H, m), 1.66 (1H, m), 1.91 (2H, m), 2.30 (1H, m), 2.56 (1H, m), 3.06 (1H, d, *J* 7), 6.01 (1H, d, *J* 3, bridgehead methine) and 7.24–7.97 (9H, m, Ar-H); *m/z* 354 (M^+), 169, 141, 115 and 77 (1, 100, 50, 17 and 21%).

Synthesis of 5-iodo-1-phenylsulfonylpent-1-ene

Pent-4-en-1-ol (4.5 g, 52 mmol), *tert*-butyldimethylsilyl chloride (8.66 g, 57 mmol) and imidazole (3.5 g, 52 mmol) in dimethylformamide (180 ml) were stirred together under argon at room temperature (20 h). After aqueous work up, chromatography on silica (150 g) in light petroleum (60–80 °C) gave the silyl ether (8.92 g, 86%); δ_H(300 MHz) 0.06 (6H, s), 0.90 (9H, s), 1.62 (2H, q, *J* 7), 2.12 (2H, q, *J* 7), 3.63 (2H, t, *J* 6), 5.04 (2H, m, methylene-H) and 5.83 (1H, tdd, *J* 7 and 14); *m/z* 143, 113, 101 and 85 (55, 13, 10 and 8%).

To a degassed solution of the protected alcohol (300 mg, 1.5 mmol) in dry carbon tetrachloride (10 ml) was added $PhSeSO_2Ph$ (668 mg, 2.2 mmol). This solution was irradiated through Pyrex (15 min) using a water cooled Hanovia lamp (125 W) placed 5 cm away from the side of the flask. The solvent was removed under reduced pressure and the yellow residue was taken up into dichloromethane (6 ml), cooled to 0 °C and aqueous hydrogen peroxide (30%, 6 ml) added with vigorous stirring. After 30 min the reaction mixture was allowed to warm to room temperature and poured into a 5% aqueous sodium hydrogen carbonate (5 ml)–dichloromethane (3 ml) mixture. The organic phase was washed with more aqueous sodium hydrogen carbonate and then water, dried ($MgSO_4$) and evaporated under reduced pressure to give an oil. Chromatography on silica, eluting with light petroleum–ether (7:3) gave 5-tert-*butyldimethylsilyloxy*-1-*phenylsulfonylpent*-1-*ene* as a colourless oil (390 mg, 79%); ν_{max}(film)/cm^{-1} 1632, 1318 and 1156; δ_H(300 MHz) 0.01 (6H, s), 0.86 (9H, s), 1.66 (2H, q, *J* 7), 2.33 (2H, q, *J* 7), 3.59 (2H, t, *J* 6), 6.32 (1H, d, *J* 15), 7.02 (1H, td, *J* 7 and 14), 7.55 (3H, m, SO_2Ph) and 7.87 (2H, d, *J* 7, SO_2Ph); *m/z* 339 ($M^+ - 1$), 283, 199 and 135 (10, 100, 6 and 43%).

The foregoing silyl ether (100 mg, 0.29 mmol), hydrogen fluoride (40% aqueous, 0.5 ml), dichloromethane (2.5 ml) and acetonitrile (2.5 ml) were stirred at 20 °C under argon (30 min). After the usual work up, chromatography on silica (30 g) in light petroleum–ether (3:1) gave 5-*hydroxy*-1-*phenylsulfonylpent*-1-*ene* as a colourless oil (66 mg, 70%); ν_{max}(film)/cm^{-1} 3300–3500 (br); δ_H(300 MHz) 1.72 (2H, quintet, *J* 7), 2.08 (1H, s, OH), 2.37 (2H, q, *J* 7), 3.65 (2H, t, *J* 6), 6.35 (1H, d, *J* 14, vinyl sulfone), 7.01 (1H, m, vinyl sulfone), 7.51–7.61 (3H, m, SO_2Ph) and 7.86 (2H, d, *J* 7, SO_2Ph); 226 (M^+), 208, 195, 214, 84 and 77 (2, 13, 16, 52, 100 and 45%).

The foregoing alcohol was converted into the toluene-*p*-sulfonate in the usual way [tosyl chloride–pyridine, 0 °C (24 h)]. After the usual work up, chromatography on silica in light petroleum–ether (4:1) gave the *toluene*-p-*sulfonate* (81%) (Found: M^+, 380.0752. $C_{18}H_{20}O_5S_2$ requires M^+, 380.0742); ν_{max}(film)/cm^{-1} 1625, 1360 and 1145; δ_H(300 MHz) 1.90 (2H, quintet, *J* 7), 2.37 (2H, q, *J* 7), 2.45 (3H, s), 4.05 (2H, t, *J* 7), 6.30 (1H, d, *J* 14, vinyl sulfone), 6.87 (1H, m, vinyl sulfone), 7.38 (2H, d, *J* 7, Ar-H), 7.60 (3H, m, Ar-H), 7.75 (2H, m, Ar-H), 7.85 (2H, m, SO_2Ph); *m/z* 380 (M^+), 244, 195, 143, 125, 84 and 77 (1, 12, 44, 34, 76, 100 and 99%).

With sodium iodide (2.55 mmol) in boiling acetone (15 ml) over 20 h the foregoing toluene-*p*-sulfonate (1.02 mmol) gave, after the usual work up and chromatography on silica in light petroleum–ether (1:1), 5-*iodo*-1-*phenylsulfonylpent*-1-*ene* as a colourless oil (260 mg, 76%) (Found: M^+, 335.9681. $C_{11}H_{13}IO_2S$ requires M^+, 335.9697); ν_{max}(film)/cm^{-1} 1620; δ_H(300 MHz) 1.98 (2H, quintet, *J* 7), 2.39 (2H, q, *J* 7), 3.16 (2H, t, *J* 7), 6.42 (1H, d, *J* 14, vinyl sulfone), 6.94 (1H, m, vinyl sulfone), 7.52–7.89 (5H, m, SO_2Ph); *m/z* 336 (M^+), 209, 141, 125 and 77 (1, 100, 15, 65 and 60%).

Alkylation of ethylene acetal 15 with 7d

To a stirred solution of the ester **15** (100 mg, 0.42 mmol) in dry THF (5 ml) at 0 °C under argon was added potassium bis(trimethylsilyl)amide in THF (0.5 mol dm^{-3}, 0.92 ml) and the mixture was stirred for 10 min. HMPA (0.1 ml) was added followed immediately by the iodide **7d** (156 mg, 0.46 mmol). The mixture was allowed to warm to room temperature before being quenched with water and extracted into ether. The organic layer was washed with 2 M hydrochloric acid and then water, dried ($MgSO_4$) and concentrated under reduced pressure. The acetal was not isolated but was cleaved to the aldehyde as follows. The acetal in THF (1 ml), water (1 ml) and 2 M hydrochloric acid (1 ml), were stirred under argon (2 h), extracted into ether and washed with water, dried ($MgSO_4$) and evaporated under reduced pressure to give an orange oil. Chromatography on silica (25 g) in benzene–ether (9:1) gave the impure cyclopropane derivative **26** as a pale yellow oil (8 mg, 4%); ν_{max}(film)/cm^{-1} 1738 and 1700; δ_H(300 MHz) −0.03 (1H, m), 0.165 (1H, m), 0.30–0.35 (2H, m), 1.15 (1H, m), 1.21 (3H, t, *J* 7.0), 2.04 (1H, m), 3.22 (1H, dd, *J* 5, 14.5), 3.35 (1H, dd, *J* 14.5, 5.5), 4.1–4.2 (2H, m, $CO_2CH_2CH_3$), 5.23 (1H, d, *J* 8.0), 7.3–7.9 (9H, m, Ar-H) and 10.31 (1H, s, CHO); the COSY spectrum established coupling of the protons at the following resonances: δ 5.23 to 2.04; 2.04 to 5.23, 3.22, 3.35 and 1.15; 1.15 to 2.04, 0.3–0.5, 0.165 and −0.03; *m/z* 527 (M^+), 389, 258, 184, 118 and 77 (1, 37, 36, 46, 77 and 100%). Further elution of the column gave *ethyl* 2-(2-*formylphenyl*)-2-(2-*phenylsulfonylcyclopent*-1-*yl*)-*acetate* **22** (80 mg, 47%) (Found: M^+, 400.1344. $C_{22}H_{24}SO_5$ requires *M*, 400.1342); ν_{max}(film)/cm^{-1} 1733, 1698, 1308 and 1148; δ_H(C_6D_6, 300 MHz) 0.73 (3H, t, *J* 7), 1.75 (3H, m), 2.01 (1H, m), 2.30 (2H, m), 3.22 (1H, m), 3.49 (1H, m), 3.80 (2H, m, $CO_2CH_2CH_3$), 5.28 (1H, d, *J* 10), 6.75 (5H, m, Ar-H), 7.10 (1H, m, Ar-H), 7.30 (1H, m, SO_2Ph), 7.55 (2H, m, SO_2Ph) and 9.78 (1H, s, CHO); *m/z* 400 (M^+), 399, 353, 211, 184, 166, 157, 91 and 77 (2, 6, 65, 100, 92, 83, 52, 61 and 90%).

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