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CYCLOADDITIONS OF SUBSTITUTED BENZOPYRAN-4-ONES TO ELECTRON-RICH DIENES: A NEW ROUTE TO XANTHONE DERIVATIVES

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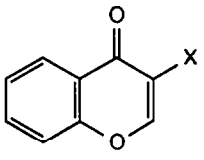
Abstract: The benzopyranones **1** and **3** reacted with 2,3-dimethyl-1,3-butadiene in the presence of titanium (IV) chloride to give the corresponding (4 + 2) cycloadducts **8** and **11**, the former undergoing facile deformylation to give **9** and **10**. Compounds **1**, **3**, and **4** underwent efficient uncatalysed cycloaddition to 1-methoxy-3-(trimethylsilyloxy)-1,3-butadiene **12** to give the respective adducts **13**, **14**, and **18** as mixtures of C-1 stereoisomers. Heating the 3-arylsulphinylchromone **5** with the diene **12** afforded 3-hydroxyxanthone **23** in 50% yield, the presumed cycloaddition - elimination sequence constituting a new route to xanthone systems. Desilylation of **13**, **14**, and **18** in acidic media provided **25**, **26**, and **27** respectively.

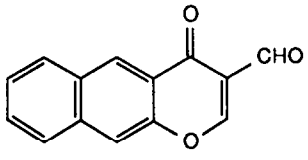
Chromones bearing electron withdrawing substituents at C-3 are highly functional molecules, capable of reacting as Michael acceptors[1,2] or heterodienes,[3] and undergoing various rearrangements on treatment with nucleophiles.[4] However, their use as 2π components in (4 + 2) cycloadditions has received surprisingly little attention[5] despite their obvious potential in such a rôle. We have therefore studied the reactions of 2,3-dimethyl-1,3-butadiene and 1-methoxy-3-(trimethylsilyloxy)-1,3-butadiene (Danishefsky's diene) with the representative pyranone systems **1** - **5**. Our results, herein described, confirm that



1 X = CHO

2 X = CO_2H

3 X = CO_2Me



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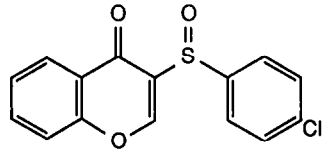

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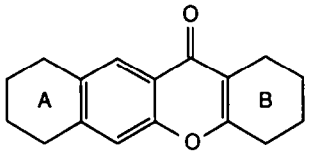

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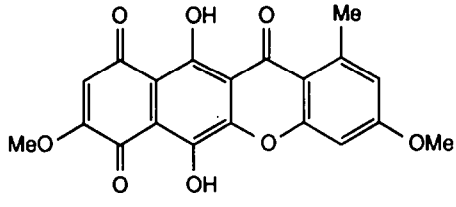

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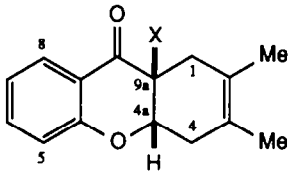
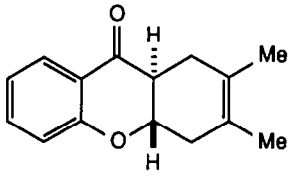
such compounds can be used as dienophiles, and that their cycloadditions offer a new synthetic route to heterocycles of the general form **6** (aromatic ring A or B or both). Compounds of this type have potential applications in approaches to xanthone-based analogues of the anthracycline antitumour agents,[6] or the antiprotozoal and antitumour benzo[*b*]xanthenone derivative bikaverin 7.[7]

Initial experiments were carried out using 2,3-dimethyl-1,3-butadiene. On treatment of the aldehyde **1** with a 10-fold excess of the diene in refluxing dichloromethane, no reaction could be detected after several days, while the inclusion of a catalytic amount of titanium(IV) chloride in the solution resulted in the formation of a complex mixture as judged by thin layer chromatography (t.l.c.). It was suspected that the initial adduct **8**, a tertiary β-ketoaldehyde, would be prone to deformylation under the conditions of the reaction; indeed, increasing the reaction temperature (so as to encourage the deformylation process) produced a cleaner mixture from which the tricycles **9** and **10** (total 41%) were isolated. With the acid **2** similar problems were encountered, the reaction requiring $TiCl_4$ catalysis and producing a complex mixture of products. However, under the same conditions the ester **3** and 2,3-dimethyl-1,3-butadiene cleanly gave the stable cycloadduct **11** (84%).



8 X = CHO



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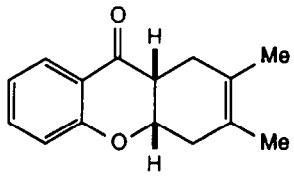

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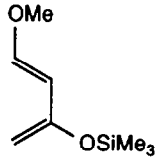
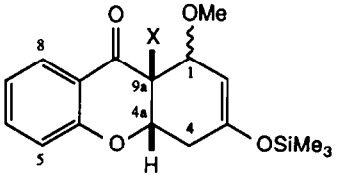
11 $X = CO_2Me$

Cycloadditions of **1** and **3** with Danishefsky's diene **12** proceeded at significantly different rates but did not require Lewis acid catalysis. Using a 5-fold excess of the diene at room temperature in dichloromethane, the aldehyde **1** gave an essentially quantitative yield of the isomeric cycloadducts **13** after a few hours, as judged by ^1H n.m.r. spectroscopy. Integration of the signals attributable to the methoxyl (δ 3.1 and 3.3 ppm) and aldehydic (δ 9.9 and 10.0 ppm) protons of each adduct indicated that there had been no useful stereoselection during the cycloaddition (isomer ratio ≤ 1.5:1). With the chromone ester **3** the diene **12** furnished a similar mixture of adducts **14**, although in this case the reaction took several days



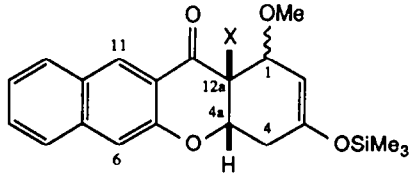
12



13 X = CHO

14 $X = CO_2Me$

22 $X = S(O)C_6H_4Cl$



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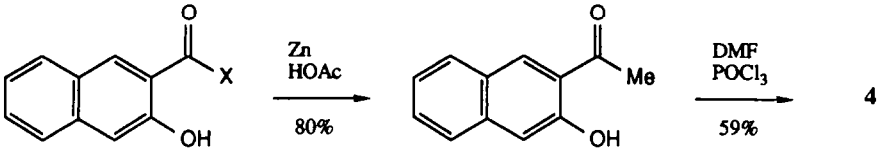


16 $X = CH_2S(O)Me$

15 X = OMe

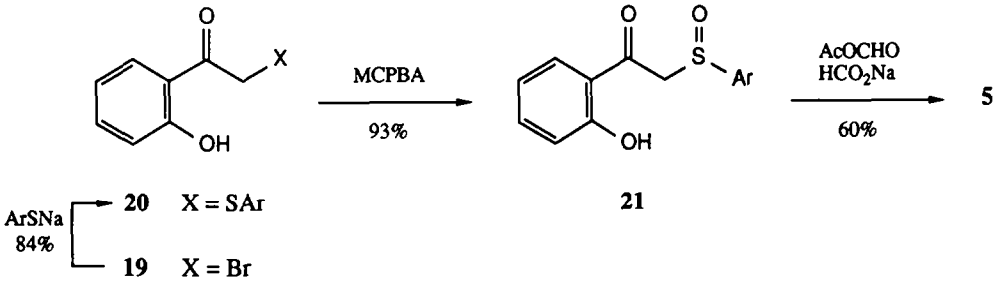
17

4

Scheme 1

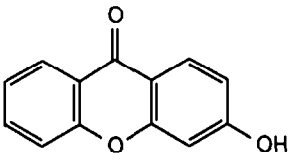
to go to completion. The reaction of the naphthopyran aldehyde **4**, prepared using established methods as shown in Scheme 1, with **12** was entirely analogous to that of its homologue **1**, producing within a few hours a mixture of the isomeric cycloadducts **18**.

It was important to determine whether 3-arysulphinylchromones could function as dienophiles, since their availability in optically active form[2] makes them potentially useful for chiral induction purposes. The reaction of the sulphoxide **5**, prepared as outlined in Scheme 2, with the diene **12** was therefore examined. Using the conditions described above resulted

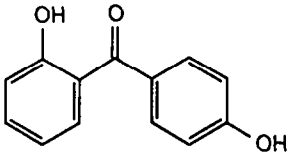


Scheme 2 (Ar = 4-Chlorophenyl)

in the slow (*ca.* 12 days) disappearance of the starting material. The instability of the products precluded their isolation and characterisation, but strong evidence for the formation of the expected adducts **22** was obtained by repeating the reaction at 85 - 90 °C. Under these circumstances the sulphoxides **22** were expected to aromatise *via* the *syn*-elimination of chlorobenzenesulphenic acid and 1,4-elimination of methanol, and indeed after 18 hours the xanthone **23** was isolated from the reaction mixture in 50% yield. This presumed cycloaddition - elimination sequence constitutes a convenient new route to xanthone derivatives.



23



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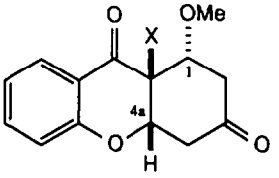
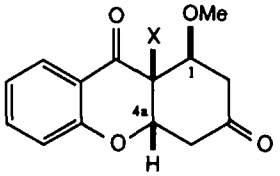
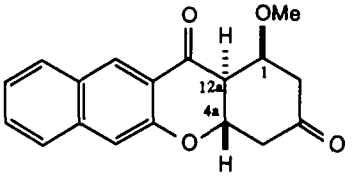


25 X = CHO



26 X = CO_2Me



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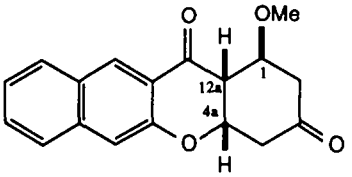

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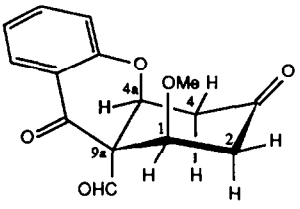
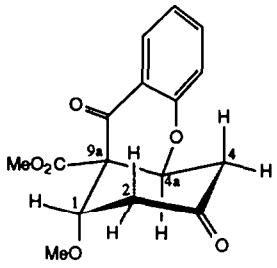
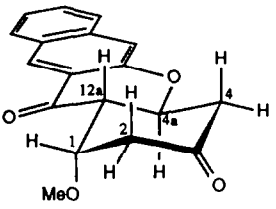
Although they decompose on standing at room temperature, the cycloadducts **13**, **14**, and **18** could be desilylated to give stable derivatives. Treatment of **13** with tetrabutylammonium fluoride gave the benzophenone **24** (44%), a result which again reflects the ease with which tertiary β-ketoaldehydes undergo deformylation. In this case the rather basic desilylating agent also provokes elimination and hence aromatisation. Such eliminations were minimised on desilylating with aqueous HF in acetonitrile.[8] Treatment of the mixture of adducts **13** with this reagent gave several products of which **25** (45%) was isolated; the sensitivity of the latter compound to base was confirmed by heating it with ethanolic sodium acetate, which gave **24** in quantitative yield. The ester adducts **14** gave a mixture on treatment with aqueous HCl in tetrahydrofuran, the product isolated in this case being **26** (22%), while flash chromatography of the complex mixture obtained on treating **18** with the HF



25'



26'



27'

reagent yielded a deformylated compound thought to be **27** (45%). The relative stereochemistry of **25** and **26** was evident from their respective ^{1}H n.m.r. spectra. In that of the aldehyde **25**, the signals due to H-1 (4.51 ppm) and H-4a (5.17 ppm) appear as narrow multiplets, and the fact that neither incorporates a large coupling to its adjacent methylene system indicates that neither is axially disposed. Decoupling reveals that there is also a 'W'-coupling of 1.9 Hz between these methines, confirming their diequatorial arrangement as depicted in **25'**. The spectrum of the ester **26** includes a narrow triplet due to H-1 at 4.59 ppm, but the signal due to H-4a at 5.47 ppm displays a 10 Hz coupling to one of the H-4 methylene hydrogens; these features are consistent with H-1 and H-4a being equatorial and axial respectively, as in **26'**. In the n.m.r. spectrum of **27**, the signal due to H-12a at 2.94 ppm (dd, *J* 2.1 and 12.5 Hz) is consistent with a 1,2-diaxial relationship with only one of the two adjacent methine hydrogens H-1 and H-4a. This indicates a *trans* relationship between these two, but their respective chemical shifts (4.59 and 4.89 ppm) are a little too close for the assignment to be unequivocal. However, reversal of this assignment would require that the structure be **28**, which with the *cis* ring fusion seems unlikely for thermodynamic reasons. The stereochemistry of the product is therefore assumed to be as indicated in **27'**.

From a synthetic viewpoint the results with Danishefsky's diene **12** are particularly significant, since Stoodley and his coworkers have recently developed a diastereoselective method for constructing the saturated A-ring of anthracyclines *via* carbohydrate-derived analogues of this diene.[9] With an appropriate naphthopyranone dienophile, it may be possible to use a similar protocol in approaches to xanthone-based analogues of these anticancer antibiotics, while the use of a chiral arylsulphinyl activating substituent on the dienophile offers a complementary route to such systems.

EXPERIMENTAL

Melting points are uncorrected. Unless otherwise stated, i.r. spectra were of liquid paraffin mulls on sodium chloride plates, recorded on Perkin-Elmer 297 or Pye-Unicam SP3-100 spectrometers. ^{1}H N.m.r. spectra were measured for solutions in deuteriochloroform unless otherwise indicated, with tetramethylsilane as the internal standard, on Varian EM 360 (60 MHz), Varian CFT-20 (80 MHz), Perkin-Elmer R32 (90 MHz), or Bruker AC300 (300 MHz) instruments. Mass spectra were measured on a Kratos MS30 instrument with a 70 eV electron impact source unless otherwise indicated, and the peak abundances are quoted as a percentage of the base peak.

2,3-Dimethyl-1,3-butadiene (Aldrich) and 1-methoxy-3-(trimethylsilyloxy)-1,3-butadiene **12** (Lancaster) were used as supplied. Other materials and solvents were routinely purified by conventional techniques.[10] Organic solutions were dried using anhydrous magnesium sulphate and concentrated by rotary evaporation. T.l.c. was carried out on Camlab Polygram SIL G/UV$_{254}$ silica gel plates, and preparative column chromatography[11] was carried out using 60H silica gel (Merck 9385). Compositions of solvent mixtures are quoted as ratios of volume. 'Petroleum' refers to a light petroleum fraction, b.p. 40 - 60 °C, unless otherwise stated.

4-Oxo-4H-1-benzopyran-3-carboxylic acid **2**. - A stirred mixture of chromone-3-carboxaldehyde **1**[12] (0.5 g, 2.9 mmol), sulphuryl chloride (0.25 ml, 3 mmol), and a few crystals of 2,2'-azobis(2-methylpropionitrile) in carbon tetrachloride (25 ml) was heated under reflux for 3 h. The cooled mixture was evaporated to dryness under reduced pressure and the residue treated with water (30 ml). Filtration, washing with water and ether, and drying under suction gave the *title compound* **2** (0.37 g, 68%) as a colourless solid, m.p. 201 - 203 °C (dec.)(ethyl acetate) (lit.[13] 204 - 205 °C), identical (i.r., n.m.r.) to material prepared by the published method.[13]

Methyl 4-oxo-4H-1-benzopyran-3-carboxylate **3**. - A mixture of the acid **2** (1.52 g, 8.0 mmol) and 3% methanolic hydrogen chloride[14] (80 ml) was stirred at room temperature for 24 h. The solution was concentrated under reduced pressure and then diluted with dichloromethane (50 ml). The mixture was washed with water, saturated aqueous sodium hydrogen carbonate, and brine, dried, and filtered. After evaporation the residue was chromatographed [dichloromethane - ethyl acetate (19:1)] to obtain the *title compound* **3** (1.43 g, 88%). Crystallisation from ethyl acetate - petroleum ether (1:3) gave a sample with m.p. 93 - 94 °C (Found: C, 64.6, H, 3.85; $C_{11}H_8O_4$ requires C, 64.7, H, 3.95%); ν_{max} 1700, 1650, and 1610 cm^{-1}; δ (60 MHz) 4.0 (3 H, s, CO_2Me), 7.25 - 7.5 (3 H, m, 6-H, 7-H, 8-H), 8.3 (1 H, dd, *J* 2.5, 8.5 Hz, 5-H), and 8.74 (1 H, s, 2-H); m/z 204 (M^+, 39%), 173 (90), 146 (100), and 121 (78).

Preparation of 4-Oxo-4H-1-naphtho[2,3-c]pyran-3-carboxaldehyde **4** *(Scheme 1).*

2-Hydroxy-3-[(methylsulphinyl)acetyl]naphthalene **16**. - Using established methodology,[15] a vigorously stirred solution of sodium hydride (100%; 1.4 g, 60 mmol) in dimethylsulphoxide (60 ml) under argon was heated in an oil bath (75 - 80 °C) for 6 h. The resulting solution was cooled in an ice bath and, with vigorous stirring, treated with methyl 3-hydroxy-2-naphthoate **15**[16] (4.04 g, 20 mmol). The resulting brown solution was stirred at room temperature for a further 0.5 h and poured into ether (200 ml), whereupon an oily solid separated out. The ether layer was decanted off and the residue triturated with a small quantity of ethanol and more ether to give a filterable yellow solid. This was collected, dissolved in water (50 ml), and treated dropwise with glacial acetic acid to precipitate out the desired sulphinyl compound **16**, which was collected by filtration and dried *in vacuo* over silica gel. The material thus obtained (3.47 g, 70%) had m.p. 186 - 188 °C, and was used without further purification.

2-Acetyl-3-hydroxynaphthalene **17**. - The crude sulphinyl compound **16** (2.98 g, 12 mmol) in glacial acetic acid (20 ml) was treated with zinc dust (5.2 g, 80 mmol), and the resulting suspension stirred vigorously at room temperature for 18 h. The mixture was then filtered through Celite and the residue washed with ethyl acetate (4 x 20 ml). The combined organic filtrate and washings were then extracted with water (200 ml portions) until the aqueous extracts did not effervesce on treatment with solid sodium hydrogen carbonate. The organic phase was dried and evaporated to give crude *2-acetyl-3-hydroxynaphthalene* **17** as a yellow solid (1.79 g, 80%), m.p. 112 - 114 °C [lit.[17] 110 - 112 °C (hexane)]; ν_{max} 1655 cm^{-1} (lit.[17] 1651 cm^{-1}); δ (60 MHz) 2.7 (3 H, s, Me), 7.0 - 7.9 (5 H, m, ArH), 8.2 (1 H, s, 1-H), and 11.5 (1 H, s, OH).

4-Oxo-4H-1-naphtho[2,3-c]pyran-3-carboxaldehyde **4**. - A solution of 2-acetyl-3-hydroxynaphthalene **17** (1.86 g, 10 mmol) in *N,N*-dimethylformamide (30 ml) at room temperature was treated with phosphorus oxychloride (4 ml), and the mixture stirred at 50 °C (bath) for 4 h. After cooling, the reaction mixture was poured on to ice water (100 ml) and stirred until a solid had formed. The solid was collected on a filter, washed with water (4 x 25 ml), and dried. The crude material was crystallised from ethyl acetate to give the *title compound* **4** (1.33 g, 59%) as plates, m.p. 222 - 224 °C (lit.[18] 220 - 222 °C); ν_{max} 1690 and 1650 cm^{-1}; δ (80 MHz, d_6-acetone) 7.55 - 7.8 (2 H, m, ArH), 8.05 - 8.30 (3 H, m, ArH), 8.70 (1 H, s, 5-H), 8.80 (1 H, s, 2-H), and 10.25 (1 H, s, CHO).

Preparation of 3-(4-Chlorophenylsulphinyl)-4H-1-benzopyran-4-one **5** *(Scheme 2).*

2-(4-Chlorophenylthio)-2'-hydroxyacetophenone **20**. - To a solution of 2-bromo-2'-hydroxyacetophenone **19**[19] (3.2 g, 15 mmol) in dioxan (5 ml) was added dropwise at room temperature a solution of sodium 4-chlorothiophenoxide [from sodium (0.35 g, 15.2 mmol) and 4-chlorothiophenol (2.2 g, 15.2 mmol)] in absolute ethanol (10 ml). After stirring for a further hour the mixture was treated with water (30 ml) and the resulting precipitate collected by filtration. Washing with water, drying by suction, and crystallisation from dichloromethane - petroleum gave the *title compound* **20** (3.5 g, 84%) as colourless needles, m.p. 83 - 84 °C (Found: C, 60.3; H, 4.1. $C_{14}H_{11}ClO_2S$ requires C, 60.3; H, 4.0%); ν_{max} 1625 and 1605 cm^{-1}; δ (60 MHz) 4.22 (2 H, s, CH_2), 6.7 - 7.9 (8 H, m, ArH), and 11.85 (1 H, s, exchanges with D_2O, OH); m/z 280 [M^+ (^{37}Cl), 21%], 278 [M^+ (^{35}Cl), 53], and 121 (100).

2-(4-Chlorophenylsulphinyl)-2'-hydroxyacetophenone **21**. - To a stirred solution of the acetophenone **20** (1.40 g, 5 mmol) in dichloromethane (10 ml) was added dropwise at 0 °C a solution of 3-chloroperoxybenzoic acid (1.1 g, 6.4 mmol) in dichloromethane (20 ml). The mixture was kept at 0 °C for 5 h and water (30 ml) then added. The dichloromethane layer was separated and the aqueous layer extracted with dichloromethane (3 x 30 ml). The combined organic phase was washed successively with water (2 x 50 ml), saturated aqueous sodium hydrogen carbonate (50 ml), and brine. The solution was evaporated and the residue crystallised from ether - dichloromethane to give the pure *title compound* **21** (1.36 g, 93%), m.p. 131 - 132 °C (Found: C, 57.3; H, 3.8. $C_{14}H_{11}ClO_3S$ requires C, 57.05; H, 3.8%); ν_{max} 1650, 1600, and 985 cm^{-1}; δ (60 MHz) 4.25 and 4.55 (each 1 H, d, *J* 14 Hz, CH_2), 6.7 - 7.8 (8 H, m, ArH), and 11.67 (1 H, s, exchanges with D_2O, OH); m/z 296 [M^+ (^{37}Cl), 9%], 294 [M^+ (^{35}Cl), 24], 248 (38), 246 (83), and 121 (100).

3-(4-Chlorophenylsulphinyl)-4H-1-benzopyran-4-one **5**. - A mixture of the acetophenone **21** (1.17 g, 4 mmol), acetic-formic anhydride[20] (3.5 g, 40 mmol), and anhydrous sodium formate (2.8 g, 40 mmol) was heated to 70 - 75 °C for 3 h and allowed to stand at room temperature for a further hour. Water (20 ml) was then added and the mixture extracted with dichloromethane (3 x 20 ml). The combined extracts were washed with water and brine, dried, and evaporated to obtain the crude product, which was crystallised from ethanol to afford the pure *title compound* **5** (0.72 g, 60%) as colourless crystals, m.p. 160 - 161 °C (Found: C, 59.2; H, 3.1. $C_{15}H_9ClO_3S$ requires C, 59.1; H, 3.0%); ν_{max} 1640, 1610, and 1050 cm^{-1}; δ (60 MHz) 7.25 - 8.25 (8 H, m, ArH) and 8.40 (1 H, s, 2-H); m/z 306 [M^+ (^{37}Cl), 78%], 304 [M^+ (^{35}Cl), 100], 257 (36), 255 (81), and 121 (93).

Cycloaddition of the Aldehyde **1** *to 2,3-Dimethyl-1,3-butadiene*. - To a stirred solution of chromone-3-carboxaldehyde **1** (200 mg, 1.15 mmol) in chloroform (10 ml) was added 2,3-dimethyl-1,3-butadiene (0.94 g, 11.5 mmol) followed by titanium(IV) chloride (2 drops). The mixture was heated under reflux for 96 hours and then concentrated to dryness *in vacuo*. The residue was chromatographed over silica gel [ether - petroleum, b.p. 60 - 80 °C, 1:9]. The major fraction contained trans-*2,3-dimethyl-1,4,4a,9a-tetrahydroxanthone* **9** (61 mg, 23%), which formed colourless prisms, m.p. 148 - 150 °C (ether) (Found: C, 79.0, H, 7.2; $C_{15}H_{16}O_2$ requires C, 78.9, H, 7.1%); ν_{max} (neat) 1680, 1600, and 1570 cm^{-1}; δ (90 MHz) 1.74 (6 H, s, 2 x Me), 2.5 - 2.7 (4 H, m, 1-H_2, 4-H_2), 2.85 (1 H, m, 9a-H), 4.40 (1 H, ddd, *J* 8, 8, 13 Hz, 4a-H), 6.9 - 7.1 (2 H, m, 5-H, 7-H), 7.48 (1 H, ddd, *J* 2, 8, 8.5 Hz, 6-H), and 7.90 (1 H, dd, *J* 2, 8.5 Hz, 8-H); m/z 229 (M + 1, 14%), 228 (M^+, 58), 213 (61), 198 (38), 195 (87), and 121 (100). Another fraction contained cis-*2,3-dimethyl-1,4,4a,9a-tetrahydroxanthone* **10** (47 mg, 18%), which was an oil, b.p. 115 - 120 °C (0.5 mmHg); ν_{max} (neat) 1680, 1600, and 1575 cm^{-1}; δ (60 MHz) 1.7 (6 H, s, 2 x Me), 2.05 - 3.1 (5 H, m, 1-H_2, 4-H_2, 9a-H), 4.8 (1 H, narrow m, 4a-H), 6.9 - 7.2 (2 H, m, 5-H, 7-H), 7.55 (1 H, ddd, *J* 2, 8, 8 Hz, 6-H), and 8.0 (1 H, dd, *J* 2, 8 Hz, 8-H).

Cycloaddition of the Ester **3** *to 2,3-Dimethyl-1,3-butadiene*. - To methyl 4-oxo-4*H*-1-benzopyran-3-carboxylate **3** (218 mg, 1.07 mmol) in dichloromethane (20 ml) was added 2,3-dimethyl-1,3-butadiene (820 mg, 10 mmol) followed by one drop of titanium(IV) chloride. The brown solution was monitored by t.l.c. [ethyl acetate - petroleum (1:5)], and when the ester was no longer detectable, the mixture was poured into water (25 ml) and the aqueous layer extracted with dichloromethane (2 x 20 ml). The combined organic phase was dried and evaporated. Flash chromatography of the residue [ethyl acetate - petroleum (1:6)] gave *methyl* cis-*1,4-dihydro-9-oxo-3-[(trimethylsilyl)oxy]xanthene-9a-carboxylate* **11** (257 mg, 84%) as a colourless oil (Found: C, 71.1, H, 6.5; $C_{17}H_{18}O_4$ requires C, 71.3, H, 6.3%); ν_{max} (neat) 1740 and 1685 cm^{-1}; δ (60 MHz) 1.7 (6 H, br s, 2 x Me), 2.2 - 2.6 (4 H, m, 1-H_2, 4-H_2), 3.75 (3 H, s, CO_2Me), 5.1 (1 H, t, *J* 4 Hz, 4a-H), 6.9 - 7.2 (2 H, m, 5-H, 7-H), 7.4 - 7.7 (1 H, m, 6-H), and 7.95 (1 H, dd, *J* 2, 8 Hz, 8-H).

General Procedure for the Cycloadditions of **1**, **3**, *and* **4** *to the Diene* **12**. - To a magnetically stirred solution of **1** or **3** (or a suspension of **4**) (1.0 mmol) in dichloromethane (5 ml) was added the diene **12** (5 mmol). To monitor the reactions, aliquots were removed periodically, concentrated *in vacuo* (room temperature, ≤ 0.5 mmHg), and the residual oil examined by ^1H n.m.r. spectroscopy. Under these conditions the aldehydes **1** and **4** were consumed within 6 - 8 h, whereas the ester **3** was still detectable [δ (90 MHz) 8.78 (s, 2 H)] after 72 - 96 h. In each case the signals characteristic of methoxy and/or aldehyde groups indicated that two cycloadducts had been formed in ratios ≤ 1.5:1.

The mixture of cycloadducts **13** had δ (60 MHz) 0.2 (total 9 H, 2 x s, $SiMe_3$), 2.5 - 2.8 (2 H, br m, 4-H_2), 3.1 and 3.3 (total 3H, both s, OMe), 4.6 and 4.75 (total 1 H, both d, *J ca.* 6 Hz, 1-H), 5.0 - 5.7 (2 H, m, 2-H, 4a-H), 6.9 - 8.1 (4 H, m, ArH), and 9.9 and 10.0 (total 1 H, both s, CHO); ν_{max} (neat) 1730 and 1675 cm^{-1}.

The mixture of cycloadducts **14** had δ (90 MHz) 0.3 (2 x s, $SiMe_3$), 2.5 - 2.6 (br m, 4-H_2), 3.1 - 4.3 (m, OMe), 4.65 and 4.8 (both d, *J ca.* 6 Hz, 1-H), 5.1 - 5.8 (m, 2-H, 4a-H), and 6.9 - 8.0 (m, ArH); ν_{max} (neat) 1735 and 1675 cm^{-1}.

The mixture of cycloadducts **18** had δ (60 MHz) 0.2 (total 9 H, 2 x s, $SiMe_3$), 2.5 - 2.8 (2 H, br m, 4-H_2), 3.2 and 3.4 (total 3H, both s, OMe), 4.75 and 4.9 (total 1 H, both d, *J ca.* 5.5 Hz, 1-H), 5.1 - 5.8 (2 H, m, 2-H, 4a-H), 7.3 - 8.1 (5 H, m, ArH), 8.7 (1 H, s, 11-H), and 10.05 and 10.15 (total 1 H, both s, CHO); ν_{max} (neat) 1725 and 1675 cm^{-1}.

Cycloaddition of **5** *to the Diene* **12**. - A solution of 3-(4-chlorophenylsulphinyl)-4*H*-1-benzopyran-4-one **5** (250 mg, 0.92 mmol) and the diene **12** (90%; 1.0 ml, 4.6 mmol) in 1,2-dimethoxyethane (10 ml) under nitrogen was heated under reflux for 18 h, cooled, and stirred at room temperature with M hydrochloric acid (2 ml) for 2 h. The mixture was then treated carefully with a solution of sodium hydrogen carbonate (0.3 g) in water (3 ml), and evaporated. The residue was

extracted with dichloromethane (3 x 15 ml), washed with water (2 x 20 ml), and dried. The residue on evaporation of the solution was triturated with dichloromethane - petroleum (1:2), and the solid collected and dried *in vacuo*, giving essentially pure *3-hydroxy-9H-xanthen-9-one* **23** (87.5 mg, 50%), m.p. 253 - 254 °C (ethanol - water) (lit.[21] 246 °C); m/z 213 (M + 1, 14%), 212 (M^+, 100), 184 (19), 177 (19), 128 (10), 92 (17), and 63 (11); R_f 0.14 [ethyl acetate - dichloromethane (1:19)].

Desilylation of Cycloadducts **13** *using Tetrabutylammonium fluoride.* - Tetra-*n*-butylammonium fluoride in tetrahydrofuran (1.0 M; 1.1 ml, 1.1 mmol) was added dropwise to a stirred solution of the adducts **13** (347 mg, 1.0 mmol) in dichloromethane (10 ml), and the resulting reddish solution stirred at room temperature for 24 h. The solvents were removed *in vacuo* and the residue purified by flash chromatography [ethyl acetate - petroleum (1:3)] to give a green oil which solidified on standing. Recrystallisation gave pure *2,4'-dihydroxybenzophenone* **24** (94 mg, 44%) as colourless plates, m.p. 148 - 150 °C (acetic acid - water) (lit.[22] 150 - 151 °C); ν_{max} 3400 - 3200, 1625, 1595, 1250, 1165, 940, 855, 835, 765, 725, and 690 cm^{-1}; δ (300 MHz) 5.66 (1 H, s, 4'-OH), 6.86 (1 H, ddd, *J* 1.0, 7.0, and 8.0 Hz, 5-H), 6.91 (2 H, br d, *J* 8.6 Hz, 3'-H_2), 7.04 (1 H, dd, *J* 1.0, 8.4 Hz, 3-H), 7.47 (1 H, ddd, *J* 1.7, 7.0, and 8.4 Hz, 4-H), 7.60 (1 H, dd, *J* 1.7, 8.0 Hz, 6-H), 7.64 (2 H, dm, *J* 8.6 Hz, 2'-H_2), and 11.94 (1 H, s, 2-OH); R_f 0.52 [ethyl acetate - dichloromethane (1:9)].

Desilylation of Cycloadducts **13** *using HF in Acetonitrile.* - A solution of the cycloadducts **13** (from 1.0 mmol of **1**) in acetonitrile (5 ml) was stirred at room temperature with a solution of aqueous hydrofluoric acid (40% HF; 0.1 ml) in acetonitrile (5 ml) for 1 h. The mixture was then concentrated *in vacuo* to give an orange oil, which was chromatographed on silica gel [dichloromethane - ethyl acetate (24:1)]. A yellow fraction containing several components was triturated with ether - petroleum (2:1) to give a colourless solid, identified as (1α,4aβ,9aβ)–*1,2,4a,9a-tetrahydro-1-methoxy-3,9-dioxo-4H-xanthene-9a-carboxaldehyde* **25** (122 mg, 45%), m.p. 120 - 125 °C (dec.) [ethyl acetate - petroleum (b.p. 60 - 80 °C)] (Found: C, 65.8; H, 5.2. $C_{15}H_{14}O_5$ requires C, 65.7; H, 5.15%); ν_{max} 1730, 1674, and 1607 cm^{-1}; δ (300 MHz) 2.44 (1 H, dd, *J* 3.7, 15.0 Hz, 2-H_{ax}), 2.83 (1 H, overlapping ddd, *J* ~ 1, 2.9, and 15.0 Hz, 2-H_{eq}), 2.91 (2 H, br d, *J* 3.5 Hz, 4-H_2), 3.09 (3 H, s, OMe), 4.51 (1 H, overlapping ddd, *J* 1.9, 2.9, and 3.7 Hz, 1-H), 5.17 (1 H, overlapping ddd, *J* 1.9, 3.5, and 3.5 Hz, 4a-H), 6.95 (1 H, d, *J* 8.6 Hz, 5-H), 7.02 (1 H, overlapping dd, *J* 7.0, 7.8 Hz, 7-H), 7.47 (1 H, overlapping ddd, *J* 1.7, 7.0, and 8.6 Hz, 6-H), 7.85 (1 H, dd, *J* 1.7, 7.8 Hz, 8-H), and 9.98 (1 H, s, CHO). On decoupling at 4.51 ppm, the signal at 5.17 ppm becomes a triplet (*J* 3.5 Hz), and the signals at 2.44 and 2.83 ppm lose their couplings of 3.7 and 2.9 Hz respectively; on decoupling at 5.17 ppm, the signal at 4.51 ppm becomes an overlapping double doublet (*J* 2.9 and 3.7 Hz), and the signal at 2.91 ppm becomes a broadened singlet.

Conversion of **25** *to 2,4'-dihydroxybenzophenone* **24**. - The adduct **25** (42 mg, 0.153 mmol) and anhydrous sodium acetate (20 mg) in ethanol (2 ml) were heated to boiling for 15 min and allowed to cool. The mixture was concentrated *in vacuo* and the residue suspended in ethyl acetate. Filtration of the solution through a short column of silica gel, washing with more ethyl acetate, and concentration of the eluate gave 2,4'-dihydroxybenzophenone **24** (33 mg, 100%), identical (t.l.c., n.m.r., m.p.) with the material obtained as described above.

Desilylation of Cycloadducts **14**. - To a solution of the ester adducts **14** (from 1.0 mmol of **3**) in tetrahydrofuran (5 ml) was added aqueous hydrochloric acid (0.1 M; 0.1 ml) and the mixture stirred at room temperature for 20 h. Water (10 ml) was then added, and the solution extracted with dichloromethane (3 x 10 ml). The combined organic phase was dried, evaporated, and the residue chromatographed [ethyl acetate - petroleum (1:5)]. A fluorescent fraction was found to contain *methyl* (1β,4aβ,9aβ)–*1,2,4a,9a-tetrahydro-1-methoxy-3,9-dioxo-4H-xanthene-9a-carboxylate* **26** (68 mg, 22%), m.p. 137 - 142 °C (dec.) (ethyl acetate - petroleum) (Found: C, 63.15; H, 5.3. $C_{16}H_{16}O_6$ requires C, 63.15; H, 5.3%); ν_{max} 1730 and 1690 cm^{-1}; δ (80 MHz) 2.65 - 2.95 (4 H, m, 2-H_2, 4-H_2), 3.28 (3 H, s, OMe), 3.72 (3 H, s, CO_2Me), 4.59 (1 H, t, *J* 3.5 Hz, 1-H), 5.47 (1 H, dd, *J* 7.5, 10 Hz, 4a-H), 6.95 (2 H, t, *J* 8Hz, 5-H, 7-H), 7.47 (1 H, dt, *J* 2, 8 Hz, 6-H), and 7.79 (1 H, dd, *J* 2, 8 Hz, 8-H).

Desilylation of Cycloadducts **18**. - A solution of the cycloadducts **18** (from 1.0 mmol of **4**) in acetonitrile (5 ml) was stirred at room temperature with a solution of aqueous hydrofluoric acid (40% HF; 0.1 ml) in acetonitrile (5 ml) for 1 h. The mixture was then concentrated *in vacuo* to give an orange-red oil, which was purified by chromatography [dichloromethane

- ethyl acetate (24:1)]. A fluorescent product (R_f 0.4) was eluted in two fractions; the first crystallised on evaporation to give essentially pure (1β,4aβ,12aα)-*1,2,4a,12a-tetrahydro-1-methoxy-4H-benzo[b]xanthene-3,12-dione* **27** (93 mg); the next fraction also contained a slightly more polar yellow component which was removed by trituration with ether, giving a further sample (40 mg) of **27** (total 133 mg, 45%). The analytical sample, pale yellow needles, had m.p. 168 - 170 °C (dec.) (ethyl acetate) (Found: C, 73.0; H, 5.5. $C_{18}H_{16}O_4$ requires C, 73.0; H, 5.4%); ν_{max} 1725, 1690, 1630, 1605, 1210, 1190, 1135, 1095, 1000, 945, 890, and 760 cm^{-1}; δ (300 MHz) 2.42 (1 H, dd, *J* 2.8, 15.4 Hz, 2-H_{ax}), 2.81 (1 H, dd, *J* 11.2, 14.5 Hz, 4-H_{ax}), 2.91 (1 H, overlapping ddd, *J* 2.1, 2.5, and 15.4 Hz, 2-H_{eq}), 2.94 (1 H, dd, *J* 2.1, 12.5 Hz, 12a-H), 3.10 (1 H, ddd, *J* 2.1, 5.6, and 14.5 Hz, 4-H_{eq}), 3.31 (3 H, s, OMe), 4.59 (1 H, overlapping ddd, *J* 2.1, 2.5, and 2.8 Hz, 1-H), 4.89 (1 H, ddd, *J* 5.6, 11.2, and 12.5 Hz, 4a-H), 7.31 (1 H, s, 6-H), 7.34 (1 H, ddd, *J ca.*1, 6.8, and 8.1 Hz, 9-H), 7.49 (1 H, ddd, *J ca.*1, 6.8, and 8.2 Hz, 8-H), 7.68 (1 H, br. d, *J* 8.2 Hz, 7-H), 7.86 (1 H, br. d, *J* 8.1 Hz, 10-H), and 8.52 (1 H, s, 11-H). Line broadening on the signals for 7-H and 10-H derives from combined small couplings to 6-H and 8-H, and 9-H and 11-H respectively; m/z (methane CI) 298 (M + 2, 19.9%), 297 (M + 1, 100.0), 295 (M - 1, 14.7), 293 (5.1), 265 (16.7), 197 (6.1), and 171 (11.7); (EI) 296 (M^+, 100%), 223 (27), 210 (47), 170 (64), 142 (34), 114 (24), and 85 (42).

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