Studies of Chromenes. Part 9.[1] Syntheses of Chromenequinones

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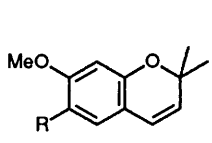
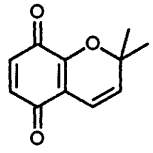
Syntheses of 2,2-dimethylchromene-5,8-quinone, 2,2-dimethylchromene-6,7-quinone, and 6,7-dimethoxy-2,2-dimethylchromene-5,8-quinone are described. Being easily bioreducible to electron-rich chromenes these compounds, and their oxirane derivatives, are of interest as possible anti-tumour alkylating agents.

The quinone–hydroquinone switch that initiates the anti-cancer chemistry of the mitomycins[2] is extensible to a range of compounds.[3] We have sought to apply the principle to the alkylating properties of chromenes related to the insect anti-juvenile hormones (**1**) and (**2**). The biological activity of the



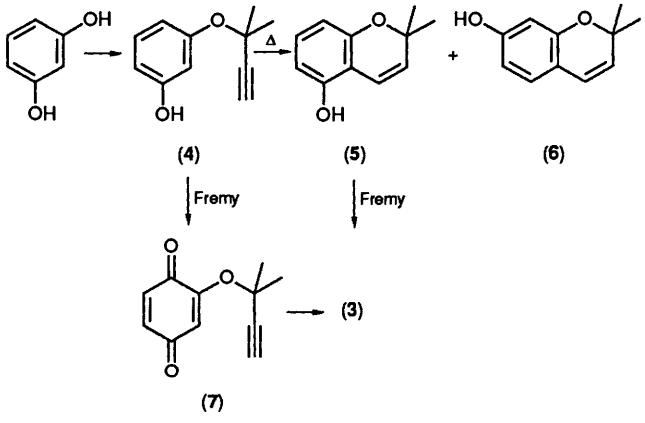
(**1**) R = H
(**2**) R = OMe



(**3**)

latter depends on their acting as suicide substrates towards an oxidase which converts them into highly reactive oxiranes and which is also involved in the biosynthesis of juvenile hormones (JH1-3).[4] This mode of action suggests that the oxiranes of electron-rich chromenes have potential as anti-tumour alkylating agents. Indeed, the chromenes themselves are of interest in this respect and just this type of chromene has recently been isolated from a traditional Chinese medicine.[5] The possibility that such chromenes, and their oxiranes, could be generated from the corresponding quinones by reduction within apoxic neoplastic tissue made the synthesis of chromenequinones relevant, our initial target being the chromene-*p*-quinone (**3**).

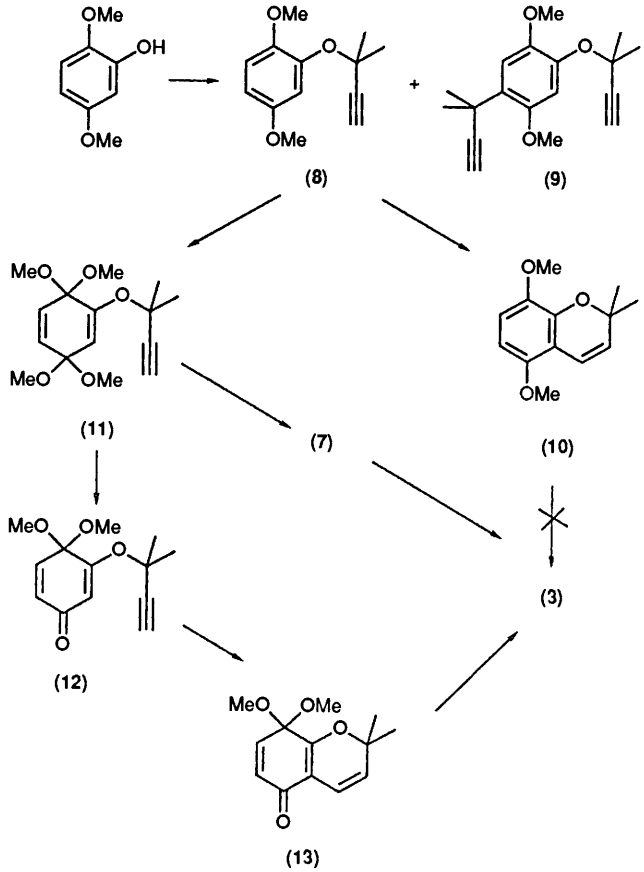
The 5,8-quinone (**3**) was synthesised by two routes. In the first (Scheme 1) thermolysis[6] of the resorcinol monoether (**4**) gave



Scheme 1.

approximately equal quantities of the two isomeric chromenes (**5**) and (**6**). The 5-hydroxychromene (**5**) was oxidised by Frémy's salt[7] to the required quinone (**3**) (90%). Frémy oxidation of the monoether (**4**) formed the quinone ether (**7**) which readily cyclised to the chromenequinone (**3**).

Formation of the monotetrahydropyranyl precursor of the monoether (**4**) was erratic so that an alternative strategy involving electrochemical oxidation[8] of a 1,4-dimethoxyarene to a quinone bisacetal was subsequently employed (Scheme 2).



Scheme 2.

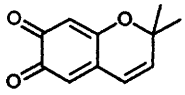
Alkylation of 2,5-dimethoxyphenol [obtained by Bayer–Villiger oxidation of 2,5-dimethoxybenzaldehyde[9] or from benzoquinone bis(dimethoxy)acetal[10]] afforded only a moderate yield of the required ether (**8**) which was accompanied by the *C*-alkylation product (**9**). Although the alkynyl ether (**8**) cyclised efficiently to the chromene (**10**) on thermolysis, oxidation of the product by either electrochemical or chemical (ceric ammonium nitrate) methods afforded only complex mixtures.

In contrast, electrolysis of the uncyclised ether (**8**) afforded the bisacetal (**11**) in excellent yield. Hydrolysis of the bisacetal gave the quinone ether (**7**) (accompanied by its cyclisation

product). Milder hydrolysis of the bisacetal allowed the isolation of the monoacetal (**12**). The structure of the latter is that expected on stereoelectronic grounds and was confirmed by nuclear Overhauser enhancement experiments. On irradiation of the acetal methyl groups one ring proton showed an enhancement of 8.6% whilst two exhibited enhancements around 2%. The monoacetal cyclised extremely rapidly to the monoacetal chromene (**13**) from which the target chromenequinone (**3**) was again obtained.

The chromene-5,8-quinone (**3**) possesses a structure in which the vinylogous ester system (–CO–CH=CH–O–) is cross-conjugated with the chromenequinone system (–CO–CH=CH–CH=CH–) so that the electron-withdrawing effect of the 8-carbonyl group on the 3,4-double bond is attenuated. We therefore synthesised the *ortho*-quinone (**14**) in which the vinylogous ester moiety may be considered as separated from the quinone alkene system and the 3,4-double bond consequently expected to be more electron-deficient.

The 7-hydroxychromene (**6**) previously obtained underwent Frémy oxidation to give the bright-red *ortho*-quinone (**14**) in



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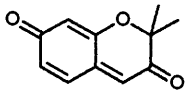

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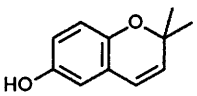

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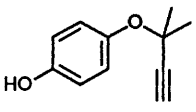

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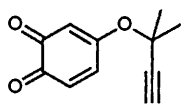

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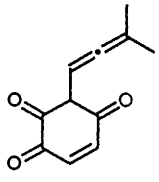

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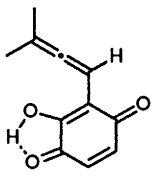

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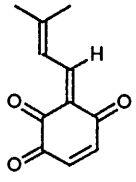


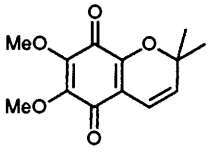
(21)

moderate yield. The alternative structure (**15**) for this product was discounted by nuclear Overhauser enhancement experiments which indicated the presence of a hydrogen at C-3 since irradiation of the gem-dimethyl groups resulted in an enhancement of 10% for one of the AB protons at δ 6.5. The other proton of the AB system (*J* 10 Hz) showed an enhancement of 5.6%. Additionally the quinone (**14**) afforded a quinoxaline derivative on reaction with phenylene-*o*-diamine. The same *o*-quinone was also obtained by Frémy oxidation of the 6-hydroxychromene (**16**) [made by thermolysis of the corresponding hydroquinone monoether (**17**)]. Oxidation of the ether (**17**) afforded an *o*-quinone ether (**18**) which readily cyclised when heated but gave only the *p*-quinone (**3**). This interesting result is seen as a consequence of the bond-fixation implicit in structure (**18**) which causes a regiospecific Claisen rearrangement to an intermediate (**19**). Regiospecific enolisation of this to the intermediate (**20**) is controlled by the greater stability of *p*-quinones (and possibly the hydrogen-bonding shown). The subsequent 1,5-hydrogen shift in turn establishes the geometry of the exocyclic double bond of the intermediate (**21**) so that electrocyclic ring closure of the latter (after rotation about the central σ-bond of the diene moiety) leads to the observed *p*-quinone (**3**).

The precocenes upon which these quinones are modelled possess methoxy groups essential to their activity, the 6,7-dimethoxychromene (**2**) being some 10 times more biologically active than the 7-methoxychromene (**1**). We therefore sought to prepare the dimethoxychromenequinone (**22**) even though the electron-withdrawing character of the quinone carbonyl groups was expected to be much reduced by their conjugation with the methoxy groups.

The chemistry of poly-oxygenated aromatics is characterised by oxidation and *ipso* substitution and in order to minimise these difficulties we introduced precursors of the quinone system into a pre-formed chromanoid. For the same reasons direct hydroxylation[11] of the chromanone (**23**) was not attempted; rather, Teuber oxidation of the 5- or 8-amino-chromanone with Frémy's salt was selected.

Nitration of the chroman-4-one (**23**) resulted in the 3-nitro-



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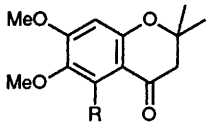
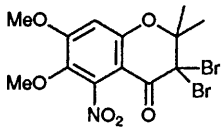


(23) R = H
(25) R = NH_2



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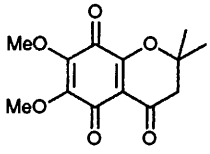

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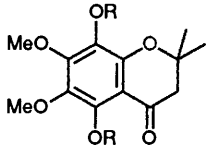
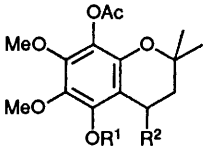


(27) R = H
(28) R = Ac



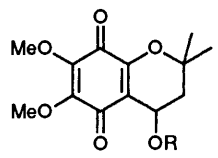
(29) $R^1 = R^2 = H$
(31) R^1 = Ac, R^2 = OAc

chromanone but this unwanted reaction could be blocked by prior bromination of the 3-methylene group. This was achieved without nuclear bromination by the use of cupric bromide.[12] The introduction of the second bromine atom was much slower than the first so that the monobromochromanone could readily be isolated if required. Nitration of the 3,3-dibromochromanone with cupric nitrate in acetic anhydride[13] afforded only a poor yield of the sole product, the 5-nitrochromanone (**24**). This structure, rather than the 8-isomer, was indicated by the disappearance of the signal at δ 7.40 (5-H) in the ^{1}H NMR spectrum of the starting material and a shift in the signal at δ 6.51 (8-H) to 6.67.

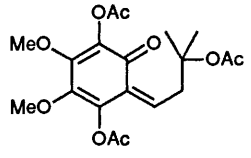
Removal of the bromine atoms and reduction of the nitro group were achieved in a single step with zinc–acetic acid in ether. The action of Frémy's salt[14] on the resultant amine (**25**) afforded the quinonoid chromanone (**26**) in excellent yield, the expected *para* quinone imine by-product also being isolated.

Mass spectrographic characterisation of quinones is complicated by the appearance of molecular ions of both the quinone and its hydroquinone due to traces of water in the inlet of the instrument[15] and led us to characterise the hydroquinone chromanone (**27**) (obtained by bisulphite reduction) as the diacetate (**28**). Reduction of the chromanone diacetate with sodium borohydride led to the selective cleavage of one of the acetoxy groups. At the same time over-reduction,[16] which could not be avoided by limiting the amount of reducing agent used, led to the formation of a chroman (**29**). No reaction occurred with the monofunctional reducing agent 9-borabicyclo-[3.3.1]nonane or on attempted catalytic hydrogenation. Fortunately chroman formation did not occur when the unacetylated hydroquinone (or quinone) was reduced, provided only the slighest excess of sodium borohydride was present.

The resultant 4,5,8-trihydroxy derivative underwent atmospheric oxidation to the quinone-4-ol (**30**) extremely easily and so was characterised as the triacetate (**31**). The latter compound was unusual in our experience in showing only a singlet for the 2-methyl groups in its 60 MHz ^{1}H NMR spectrum. We therefore considered the isomeric *ortho*-quinone methide structure (**32**) for the triacetate despite the usual colour



(**30**) R = H
(**33**) R = Ac



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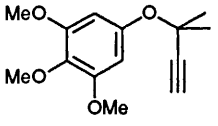

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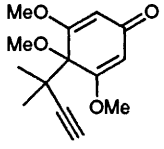

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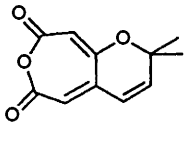

(**36**)

and instability of such compounds[17] and despite the low chemical shift of the implied vinylic-H (δ 6.00, apparent triplet). At 200 MHz the ^{1}H 2-methyl signals remained a singlet, albeit a broad one, but ring-opening was disproved by the non-equivalence of the 3-CH_2 hydrogens. These appeared as part of an ABX system, the 4-H signal being clearly a double doublet and not a triplet. The ^{13}C NMR spectrum also revealed the two 2-methyl groups to have different chemical shifts.

Oxidation of the 4,5,8-trihydroxy derivative with ferric chloride gave the quinonoid chroman-4-ol (**30**) which was also unusual in that, though the signals for the gem-methyl groups were distinct in the ^{1}H NMR spectrum, they were coincident in the ^{13}C spectrum. The acetyl derivative (**33**) showed distinct signals for the 2-methyl groups in both its ^{13}C and ^{1}H spectra. The quinone chromanol was dehydrated with toluene-*p*-sulphonic acid in boiling toluene to give the target chromene (**22**).

Despite the poor yield in the nitration step, the overall yield in this sequence is *ca.* 30% since the remaining reactions are highly efficient. Nevertheless, in attempting to devise a more direct route we briefly investigated schemes in which the aromatic substitution pattern was to be established before formation of the chromanone system; these merely served to illustrate the difficulties referred to earlier however. For example, alkylation of 3,4,5-trimethoxyphenol with 3-chloro-3-methylbut-1-yne afforded only 35% of the required ether (**34**); the remaining material (**35**) was the result of *ipso*-attack. Furthermore, nitration of the acetylenic ether (**34**) gave none of the required nitration product (which was to have been converted, after reduction, directly into an aminochromene by Claisen rearrangement[18]). Instead 3,5-dimethoxy-4-nitrophenol, again a product of *ipso*-attack, was obtained.

Treatment of the chromenequinones with 3-chloroperoxybenzoic acid was instructive in indicating the extent of electron-withdrawal from the 3,4-double bonds [as are the chemical shifts of the 3-protons, *viz.* δ 5.38, 5.50, 5.64 and 6.49 for compounds (**2**), (**22**), (**3**) and (**14**) respectively]. The 5,8-quinone (**3**) gave an isolable 3,4-oxirane indicating some degree of stabilisation compared with the precocene oxiranes themselves which are extremely reactive. The 6,7-quinone (**14**) reacted with 3-chloroperoxybenzoic acid with loss of colour to give a compound consistent with the structure (**36**), anhydrides being the usual products of peracid oxidation of α-diketones.[19] Mass spectrometry indicated the addition of a single oxygen atom without affecting either the planar symmetry of the starting material (the gem-dimethyl groups appeared as a singlet in the ^{1}H NMR spectrum) or the presence of a *cis*-double bond. This observation implies appreciable electron withdrawal from the 3,4-double bond as expected. The dimethoxychromenequinone (**22**) was rapidly decolourised by peracid but no products could be isolated. However, it did form a dibromide on treatment with *N*-bromoacetamide though the stereochemistry of this is uncertain. It appears to be a *cis*-3,4-dibromide ($J_{3,4}$ 2.6 Hz) on the basis of the 3,4-coupling constants of 3.1 and 5.2 Hz observed for the quinone 4-acetate (**30**) and ranges of 3–5 Hz (*cis*) and 5–9 Hz (*trans*) found for a number of 3,4-disubstituted chromans but the observed coupling could also indicate a *trans* configuration with both bromines axially disposed. Either stereochemistry is possible depending on the relative stabilities of intermediate carbenium and bromonium ions and the extent of steric effects. The dibromide readily lost hydrogen bromide to give a 3-bromochromenequinone whose structural assignment was based on the chemical shifts expected for bromine substitution at C-3 and C-4 of the parent chromene (**22**), the observed signal at δ 6.75 being compared with calculated values of δ 6.8 (3-Br) and 5.95 (4-Br).

Only two chromenequinones appear to be recorded in the literature[20] although there are examples of benzochromenequinones (2*H*-naphthopyrans)[21] and their dihydro derivatives (benzochromanquinones).[22] Several 5,8-dihydroxychromene[23] and their ethers[24] together with related chroman-4-ones and -4-ols are also known.[25] At the chromone oxidation level khellin is related[26] and, yet further removed, quinonoidal chalcones are known.[27]

Experimental

M.p.s (Kofler hot-stage) are uncorrected. IR spectra were recorded on a Nicolet 20 SXB FT instrument and UV spectra determined with a Perkin-Elmer Model 137 instrument. ^{1}H NMR spectra were obtained on a Brüker WP-200 spectrometer with tetramethylsilane as internal standard and ^{13}C spectra on the same machine working at 50.3 MHz. Nuclear Overhauser enhancement measurements were made on a Brüker WM300/WB spectrometer. Mass spectra were obtained on either an AEI MS9 or a Kratos MS80 instrument. Elemental analyses were performed with a Carlo Erba Model 1106 CHN machine. Homogeneity of non-crystalline compounds was established by TLC in at least three solvents of differing polarities. Ether refers to diethyl ether and light petroleum to that fraction with b.p. 40–60 °C.

3-Tetrahydropyran-2-yloxyphenol.—Freshly distilled dihydropyran (4.59 g, 4.98 ml, 54.5 mmol) was added dropwise to an ice-cold solution of resorcinol (6 g, 54.5 mmol) in ethyl acetate (20 ml) containing concentrated hydrochloric acid (4 drops). After 2 h the solution was made alkaline with aqueous sodium hydroxide and the ethyl acetate layer removed. Solid CO_2 was added to the aqueous layer which was stirred until the former had disappeared; the latter was then extracted with dichloromethane. The organic layer was dried (Na_2SO_4) and evaporated to give tetrahydropyranyl ether (2.6 g, 25%), as colourless *needles*, m.p. 90–91 °C (from chloroform–light petroleum), ν_{max}(KBr) 3 296br, 1 600 and 1 280 cm^{-1}; λ_{max}(EtOH) 221 (ε 6 000 dm^3 mol^{-1} cm^{-1}), 274 (2 250), and 280 nm (1 950); δ_H($CDCl_3$) 1.54–2.06 (6 H, m), 3.63 (1 H, m), 3.92 (1 H, m), 5.38 (1 H, t, *J* 3.3), 6.45 (1 H, ddd, *J* 8.1, 2.3 and 1.0 Hz), 6.56 (1 H, s, OH), 6.58 (1 H, dd, *J* 2.3 and 0.9 Hz) and 7.08 (1 H, dd, *J* 8.1 Hz); δ_C($CDCl_3$) 18.8, 25.2, 30.4, 62.3, 96.7, 104.2, 109.1, 109.2, 130.1, 157.0 and 158.3 (Found: C, 67.9; H, 7.25%;

M^+, 194.0964. $C_{11}H_{14}O_3$ requires C, 68.0; H, 7.3%; *M*, 194.0943).

The yield quoted is the highest obtained; much lower yields were sometimes obtained for no obvious reason.

3-Tetrahydropyran-2-yloxyphenyl 2-Methylbut-3-yn-2-yl Ether.—A solution of the above tetrahydropyranyl ether (1.5 g, 7.73 mmol) and 3-chloro-3-methylbutyne* (1.05 g, 10.0 mmol) in dry acetone (50 ml) containing dry potassium carbonate (2.0 g, 14.5 mmol), was boiled under reflux overnight in an atmosphere of nitrogen. The mixture was concentrated, partitioned between water and dichloromethane, and the organic solution washed with aqueous sodium hydroxide. Chromatography on alumina (20% dichloromethane–light petroleum containing 1% triethylamine as eluant) afforded the title ether (0.626 g, 2.41 mmol, 32%) as a colourless *oil*, ν_{max}(film) 3 286 (C≡C) and 2 113 cm^{-1} (≡CH); $\delta_H(CDCl_3)$ 1.37–2.07 (6 H, m), 1.63 (6 H, s), 2.56 (1 H, s, HC≡), 3.55 and 3.90 (each 1 H, m, OCH_2), 5.37 (1 H, t, *J* 3.3 Hz, acetal-H), 6.74 (1 H, ddd, *J* 8.2, 2.4 and 1.0 Hz), 6.85 (1 H, ddd, *J* 8.2, 2.3 and 1.0 Hz), 6.95 (1 H, dd, *J* 2.3/2.4 Hz) and 7.15 (1 H, dd, *J* 8.2 and 1.0 Hz); $\delta_C(CDCl_3)$ 19.0, 25.3, 29.7, 30.5, 62.1, 72.3, 73.8, 86.3, 96.7, 110.1, 111.2, 114.6, 129.1, 156.7 and 157.8 (Found: M^+, 260.1437. $C_{16}H_{20}O_3$ requires *M*, 260.1412).

3-(2-Methylbut-3-yn-2-yloxy)phenol (**4**).—A solution of the above bisether (0.100 g, 0.38 mmol) in methanol (10 ml) containing a catalytic amount of toluene-*p*-sulphonic acid was set aside at room temperature for 2 h. Saturated aqueous sodium hydrogen carbonate was added and the solution concentrated and extracted with dichloromethane. The organic phase was dried (Na_2SO_4) and evaporated and flash chromatography of the residue (20% ether–light petroleum as eluant) gave the title ether (**4**) as a colourless *oil* (0.065 g, 95%), ν_{max}(film) 3 383br, 3 290, 2 125, 1 594 and 1 133 cm^{-1}; $\delta_H(CDCl_3)$ 1.64 (6 H, s), 2.55 (1 H, s), 6.55 (1 H, br s), 6.57 (1 H, m), 6.78–6.82 (2 H, m), and 7.11 (1 H, apparent t, *J* and *J'* 8.6 Hz); $\delta_C(CDCl_3)$ 29.7q, 72.7s, 74.1d, 86.2d (long-range coupling, *J* 50 Hz), 109.0d, 110.4d, 113.8d, 129.6d, 156.4s and 156.7s (Found: M^+, 176.0811. $C_{11}H_{12}O_2$ requires *M*, 176.0837).

Thermolysis of the Ether (**4**).—The ether (**4**) (1.00 g, 5.68 mmol) in dry, degassed xylene (60 ml) was boiled under reflux in an atmosphere of nitrogen for 24 h. The solvent was evaporated to give a mixture of isomers (86% overall yield) which was separated by chromatography (1:1 dichloromethane–light petroleum as eluant) into two components. The first was the 5-hydroxychromene (**5**) (0.480 g, 48%) obtained as colourless needles, m.p. 138–139 °C (from ether–light petroleum) (lit.,[29] 130–133 °C), ν_{max}(KBr) 3 363br, 1 635, 1 614, 1 582 and 1 458 cm^{-1}; $\delta_H(CDCl_3)$ 1.43 (6 H, s), 4.92 (1 H, s, OH), 5.60 (1 H, d, *J* 9.9 Hz, 3-H), 6.30 (1 H, dd, *J* 8.1 and 0.9 Hz, 6-H), 6.41 (1 H, ddd, *J* 8.1, 0.9 and 0.7 Hz, 8-H), 6.63 (1 H, dd, *J* 9.9 and 0.7 Hz, 4-H) and 6.94 (1 H, apparent t, *J* and *J'* 8.1 Hz, 7-H) (Found: M^+, 176. Calc. for $C_{11}H_{12}O_2$: *M*, 176).

The second component was the 7-hydroxychromene[30] (**6**) (0.390 g, 40%) which rapidly oxidised in air and was therefore characterised as the acetate, an *oil*, ν_{max}(film) 1 764, 1 611 and 1 209 cm^{-1}; $\delta_H(CDCl_3)$ 1.44 (6 H, s), 2.26 (3 H, s), 5.57 (1 H, d, *J* 9.8 Hz, 3-H), 6.29 (1 H, d, 9.8 Hz, 4-H), 6.55 (1 H, d, *J* 2.2 Hz, 8-H), 6.56 (1 H, dd, *J* 7.9 and 2.2 Hz, 6-H), and 6.95 (1 H, d, *J* 7.9 Hz, 5-H); $\delta_C(CDCl_3)$ 21.1, 28.2, 77.8, 110.1, 113.7, 114.9, 121.7, 130.2, 151.3, 153.9 and 169.1 (Found: M^+, 218. Calc. for $C_{13}H_{14}O_3$: *M*, 218).

2,2-Dimethylchromene-5,8-quinone (**3**).—The 5-hydroxychromene (**5**) (0.560 g, 3.18 mmol) in acetone (20 ml) was added to a stirred solution of dipotassium nitrosodisulphonate[31] (Frémy's salt) (1.75 g, 6.52 mmol) in water (100 ml) containing potassium dihydrogen phosphate (0.86 g). After 6 h the solution was extracted with dichloromethane (3 × 30 ml) and the combined extracts were washed with 0.5M NaOH, dried (Na_2SO_4), and evaporated. Flash chromatography (30% ethyl acetate–light petroleum as eluant) of the residue gave the title chromene-*p*-quinone (0.490 g, 2.57 mmol, 81%). Sublimation at 80–100 °C (0.17 mmHg) afforded deep yellow *crystals*, m.p. 79–80 °C, ν_{max}(KBr) 1 672, 1 647 and 1 574 cm^{-1}; λ_{max}(EtOH) 263 (ε 16 200 $dm^3\ mol^{-1}\ cm^{-1}$) and 466 nm (1 250); $\delta_H(CDCl_3)$ 1.52 (6 H, s), 5.64 (1 H, d, *J* 10.0 Hz, 3-H), 6.43 (1 H, d, *J* 10.0 Hz, 4-H), and 6.65 (2 H, apparent s, 6- and 7-H); $\delta_C(CDCl_3)$ 28.4, 80.5, 114.8, 116.0, 130.3, 134.7, 135.9, 150.5, 181.6 and 184.3 (Found: C, 69.7; H, 5.25%; M^+, 190.0629. $C_{11}H_{10}O_3$ requires C, 69.5; H, 5.3%; *M*, 190.0630).

(2-Methylbut-3-yn-2-yloxy)-1,4-benzoquinone (**7**).—A solution of the ether (**4**) (0.580 g, 3.37 mmol) in acetone (3 ml) was slowly added to a stirred ice-cold solution of Frémy's salt (2.71 g, 1.0 mmol) in a mixture of water (360 ml) and acetone (100 ml) buffered with 0.167M aqueous potassium dihydrogen phosphate (60 ml). Stirring was continued until all starting material had reacted (8 h, TLC). The mixture was extracted with cold ethyl acetate, washed with brine, and dried ($MgSO_4$) and evaporated <5 °C. Flash chromatography of the yellow residue (20% ethyl acetate–light petroleum as eluant) gave first the chromenequinone (**3**) (0.172 g, 30%) and then the title quinone (0.258 g, 45%) which was further purified by sublimation (100 °C, 0.1 mmHg) to give a yellow *solid* which decomposed when heated, ν_{max}(KBr) 3 237, 2 112, 1 661, 1 638 and 1 613 cm^{-1}; $\delta_H(CDCl_3)$ 1.76 (6 H, s), 2.75 (1 H, s), 6.57 (1 H, dd, *J* 1.6 and 0.6 Hz, 3-H), 6.66 (1 H, dd, *J* 10.0 and 1.6 Hz, 5-H), and 6.72 (1 H, dd, *J* 10.0 and 0.6 Hz, 6-H); $\delta_C(CDCl_3)$ 28.8, 74.2, 77.3, 82.3, 112.4, 134.9, 136.6, 154.3, 182.1 and 187.7 (Found: C, 69.9; H, 5.4%; M^+, 190.0661. $C_{11}H_{10}O_3$ requires C, 69.5; H, 5.3%; *M*, 190.0630). Prolonged reaction times led to the chromene as the sole product.

2,5-Dimethoxyphenol from 2,5-Dimethoxybenzaldehyde.—2,5-Dimethoxybenzaldehyde (50 g, 0.301 mol) was added over 1 h to a stirred slurry of 3-chloroperoxybenzoic acid (70.7 g, 0.4 mol) in dry dichloromethane (500 ml) at 0 °C. The mixture was stirred overnight and then allowed to reach room temperature. The solvent was evaporated and the residue taken into ethyl acetate (600 ml) and the solution was washed with aqueous sodium metabisulphate (250 ml) and saturated aqueous sodium hydrogen carbonate (5 × 200 ml), dried ($MgSO_4$), and evaporated. The resultant formate ester was obtained as colourless *plates* (52.5 g, 0.29 mol, 96%), m.p. 61–63 °C (from ethanol), ν_{max}(KBr) 1 743 and 1 512 cm^{-1}; $\delta_H(CDCl_3)$ 3.73 (3 H, s), 3.77 (3 H, s), 6.69 (1 H, d, *J* 3.0 Hz), 6.75 (1 H, dd, *J* 8.9 and 3.0 Hz), and 6.91 (1 H, d, *J* 8.9 Hz); $\delta_C(CDCl_3)$ 55.7, 56.5, 109.2, 111.9, 113.8, 139.5, 145.0, 153.9 and 159.0 (Found: C, 59.6; H, 5.45%; M^+, 182.0608. $C_9H_{10}O_4$ requires C, 59.3; H, 5.5%; *M*, 182.0579).

Aqueous potassium hydroxide (10%; 194 ml, 0.35 mol) was added dropwise in an atmosphere of nitrogen and at room temperature to a stirred solution of the formate (52 g, 0.285 mol) in methanol (410 ml) containing sodium dithionite (3.1 g) as antioxidant. The mixture was stirred for 1 h and then neutralised with 2M aqueous hydrochloric acid and the mixture extracted with ether (3 × 300 ml). The organic solution was

* The literature preparation[28] of this chloride from the available alcohol is much improved by carrying out the reaction at −10 °C since very little intensely black material is then formed.

washed with saturated aqueous sodium hydrogen carbonate (2 × 400 ml), dried ($MgSO_4$) and evaporated. Distillation of the residue (115 °C/1.5 mmHg) (lit.,[32] b.p. 134–135 °C/15 mmHg) gave the required phenol (36 g, 0.233 mol, 82%) as an oil, ν_{max}(film) 3 426, 1 598 and 1 511 cm^{-1}; $\delta_H(CDCl_3)$ 3.74 (3 H, s), 3.80 (3 H, s), 6.0 (1 H, br s), 6.39 (1 H, dd, *J* 8.8 and 3.0 Hz), 6.60 (1 H, d, *J* 3.0 Hz) and 6.77 (1 H, d, *J* 8.8 Hz); $\delta_C(CDCl_3)$ 55.6, 56.6, 102.0, 104.4, 111.8, 141.2, 146.6 and 154.6 (Found: M^+, 154. Calc. for $C_8H_{10}O_3$: *M*, 154).

2,5-*Dimethoxyphenol from* 1,4-*Dimethoxybenzene*.—Benzoquinone bis(dimethyl) acetal, prepared by electrolysis of 1,4-dimethoxybenzene,[33] formed colourless crystals, m.p. 41–42 °C (from ether) (lit.,[34] 42.5 °C), λ_{max}(EtOH) 211 (end abs.) (ε 1 500 $dm^3\ mol^{-1}\ cm^{-1}$), 222 (1 400) and 289 nm (340); $\delta_H(CDCl_3)$ 3.30 (12 H, s) and 6.11 (4 H, s); $\delta_C(CDCl_3)$ 49.9, 93.3 and 130.4

Acetic anhydride (30 ml) containing concentrated sulphuric acid (1.2 ml) was added with stirring over 3 h to a solution of the bisacetal (63 g) in acetic acid (1.8 l) at 55 °C. Solvent was removed and the residue distilled under reduced pressure to give the 2,5-dimethoxyphenyl acetate (b.p. 82 °C/0.3 mmHg). The distillate was stirred in methanol (250 ml) containing saturated aqueous sodium hydrogen carbonate (250 ml) for 1.5 h, acidified with concentrated hydrochloric acid, and extracted with ethyl acetate. Work-up as before gave the title phenol (24 g, overall 55%).

Alkylation of 2,5-*Dimethoxyphenol*.—A method involving the use of sodium iodide[35] was used. 2,5-Dimethoxyphenol (9.72 g, 63 mmol), anhydrous potassium carbonate (10.44 g, 75.6 mmol), potassium iodide (16.7 g, 100 mmol), and 3-chloro-3-methylbutyne (12.9 g, 126 mmol) in dry acetone (105 ml) was boiled under reflux for 20 h. The mixture was filtered, the residue washed with acetone and the solution evaporated. The resultant oil was partitioned between 1M aqueous sodium hydroxide and dichloromethane and the organic phase washed with brine and dried (Na_2SO_4). Removal of the solvent left an oil which on flash chromatography (10% ethyl acetate–light petroleum as eluant) gave two fractions. The first was the bis-alkylated product 4-(2-methylbut-3-yn-2-yl)-2,5-dimethoxyphenyl 2-methylbut-3-yn-2-yl ether (**9**) (3.80 g, 13 mmol, 21%) obtained as colourless *needles*, m.p. 79–80 °C (from light petroleum); ν_{max}(KBr) 3 277, 2 111, 2 033, 1 508 and 1 207 cm^{-1}; $\delta_H(CDCl_3)$ 1.65 (6 H, s), 1.68 (6 H, s), 2.39 (1 H, s), 2.56 (1 H, s), 3.79 (3 H, s), 3.80 (3 H, s), 7.13 (1 H, s) and 7.30 (1 H, s); $\delta_C(CDCl_3)$ 29.2 (q), 29.4 (q), 35.7 (s), 55.9 (q), 56.9 (q), 69.7 (d), 73.3 (d), 74.0 (s) and 87.1 (d) (long-range coupling, *J* 50 Hz), 92.0 (d) (long-range coupling, *J* 50 Hz), 109.3 (d), 113.8 (d), 128.6 (s), 144.1 (s), 146.3 (s) and 151.4 (s) (Found: C, 76.25; H, 7.3%; M^+, 286.1545. $C_{18}H_{22}O_3$ requires C, 76.0; H, 7.1%; *M*, 286.1579.

The second component was the required 2,5-dimethoxyphenyl 2-methylbut-3-yn-2-yl ether (**8**) (4.58 g, 20.8 mmol, 33%), obtained as colourless *needles*, m.p. 39–40 °C (from light petroleum), ν_{max}(KBr) 3 245, 2 110 and 1 507 cm^{-1}; $\delta_H(CDCl_3)$ 1.65 (6 H, s), 2.56 (1 H, s), 3.73 and 3.76 (each 3 H, s), 6.55 (1 H, dd, *J* 8.9 and 3.0 Hz), 6.80 (1 H, d, *J* 8.9 Hz) and 7.11 (1 H, d, *J* 3.0 Hz); $\delta_C(CDCl_3)$ 29.4, 55.7, 56.7, 73.5, 73.9, 86.6, 108.1, 110.3, 113.5, 145.7, 147.3 and 153.7 (Found: C, 71.0; H, 7.25%; M^+, 220.1110. $C_{13}H_{16}O_3$ requires C, 70.9; H, 7.3; *M*, 220.1100).

5,8-*Dimethoxy*-2,2-*dimethylchromene* (**10**).—The above ether (**8**) (1.9 g, 9.7 mmol) was boiled under reflux in toluene overnight under an atmosphere of nitrogen. The solvent was evaporated and flash chromatography of the residue (50% dichloromethane–light petroleum as eluant) gave the required 5,8-dimethoxychromene (1.75 g, 91%) as colourless *needles*, m.p. 65 °C (from ether–light petroleum), ν_{max}(KBr) 1 637 and 1 490 cm^{-1}; $\delta_H(CDCl_3)$ 1.47 (6 H, s), 3.76 and 3.80 (each 3 H, s), 5.57 (1 H, d, *J* 10 Hz, 3-H), 6.29 [1 H, d, *J* 9 Hz, 7 (or 6)-H], 6.65 (1 H, d, *J* 10 Hz, 4-H) and 6.69 [1 H, d, *J* 9 Hz, 6 (or 7)-H]; $\delta_C(CDCl_3)$ 27.8 (q), 56.0 (q), 57.3 (q), 76.1 (s), 102.0 (d), 112.1 (s), 113.2 (d), 117.3 (d), 129.3 (d), 140.2 (s), 143.3 (s) and 149.9 (s) (Found: C, 70.85; H, 7.3%; M^+, 220.1100. $C_{13}H_{16}O$ requires C, 70.9; H, 7.3%; *M*, 220.1100).

2-(2-*Methylbut*-3-*yn*-2-*yloxy*)-p-*benzoquinone Bis*(*dimethyl*) *Acetal* (**11**).—The above ether (**8**) (0.360 g, 1.64 mmol) in 1% KOH–MeOH (50 ml) was electrolysed (constant 150 mA) overnight with stirring and water cooling using 1 cm^2 platinum electrodes. The solvent was evaporated and the residue taken up in ether/water. The aqueous layer was extracted with ether and the combined organic phases were washed with brine, dried (Na_2CO_3), and evaporated at 20 °C to give the title ether as a yellow *oil* (410 mg, 1.44 mmol, 88%); ν_{max}(film) 2 137 and 3 243 cm^{-1}; $\delta_H(CDCl_3)$ 1.67 (6 H, s), 2.63 (1 H, s), 3.21 and 3.26 (each 6 H s), 5.69 (1 H, d, *J* 2.4 Hz), 5.77 (1 H, d, *J* 10.4 Hz), and 6.09 (1 H, dd, *J* 10.4 and 2.4 Hz); $\delta_C(CDCl_3)$ 29.3, 50.2, 51.2, 71.1, 75.2, 84.5, 94.7, 97.2, 106.1, 130.8 and 131.8 (Found: M^+, 282. $C_{15}H_{22}O_5$ requires *M*, 282).

Partial Hydrolysis of the Bisacetal (**11**).—The oil (**11**) was dissolved in acetone (10 ml) and cooled to 0 °C. Aqueous acetic acid (2%) was added with stirring and the solution allowed to warm to ambient temperature. The mixture was stirred for a further 2 h. Saturated aqueous sodium hydrogen carbonate (10 ml) was added and the solution extracted with ether, dried (Na_2CO_3), and evaporated. The residue was 2-(2-methylbut-3-yn-2-yloxy)benzoquinone 1-dimethyl acetal (**12**) (0.325 g, 97%), obtained as coloured *needles*, m.p. 79–80 °C (from ether–light petroleum); ν_{max}(KBr) 3 234, 2 110, 1 670, 1 634 and 1 605 cm^{-1}; λ_{max}(EtOH) 224 (ε 10 250 $dm^3\ mol^{-1}\ cm^{-1}$) and 289 nm (5 300); $\delta_H(CDCl_3)$ 1.77 (6 H, s), 2.73 (1 H, s), 3.31 (6 H, s), 6.27 (1 H, d, *J* 1.9 Hz, 3-H), 6.33 (1 H, dd, *J* 10.2 and 1.9 Hz, 5-H), and 6.52 (1 H, d, *J* 10.2 Hz, 6-H) (on irradiation of the signal at δ 3.31 nuclear Overhauser enhancements of 8.6, 1.7, 2.4 and 1.5% were observed for the signals at δ 6.52, 6.33, 6.27 and 1.77 respectively); $\delta_C(CDCl_3)$ 29.1, 51.4, 73.8, 76.9, 82.7, 94.4, 109.3, 131.1, 141.6, 164.4 and 186.4 (Found: C, 66.3; H, 6.75%; M^+, 236.1038. $C_{13}H_{16}O_4$ requires C, 66.1; H, 6.8%; *M*, 236.1049).

2-(1,1-*Dimethylpropynyl*)-5-(2-*methylbut*-3-*yn*-2-*yloxy*)-*benzoquinone* 4-*Dimethyl Acetal*.—The ether (**8**) (6.05 g), containing *ca.* 5% (by NMR) of the *C*-alkylated product, was electrolysed and partially hydrolysed as above. Flash chromatography of the crude product (10% ethyl acetate–light petroleum) gave, in addition to the required monoacetal (**12**), the title monoacetal derived from the *C*-alkylated impurity (0.346 g) as pale yellow *needles*, m.p. 116–118 °C (from ether–light petroleum), ν_{max}(film) 2 116, 1 677, 1 650 and 1 591 cm^{-1}; $\delta_H(CDCl_3)$ 1.59 (6 H, s), 1.73 (6 H, s), 2.38 (1 H, s), 2.70 (1 H, s), 3.26 (6 H, s), 6.16 (1 H, s, 6-H) and 6.80 (1 H, s, 3-H) (irradiation of the signal at δ 3.26 led to nuclear Overhauser enhancements of 2.1 and 9.3% for the signals at δ 6.16 and 6.80 respectively); $\delta_C(CDCl_3)$ 28.8 (q), 29.1 (q), 35.5 (s), 51.3 (q), 71.3 (d), 73.6 (s), 76.7 (d), 82.8 and 89.8 (each d, long-range coupling, *J* 50 Hz), 95.1 (s), 110.4 (d), 137.5 (d), 143.9 (s), 162.9 (s) and 185.0 (s) (Found: C, 71.55; H, 7.3%; M^+, 302.1498. $C_{18}H_{22}O_4$ requires C, 71.5; H, 73.%; *M*, 302.1517.

2,2-*Dimethylchromene*-5,8-*quinone* 8-*Dimethyl Acetal* (**13**).—The ether monoacetal (**12**) (0.780 g, 3.3 mmol) in acetone (25 ml) was boiled under reflux for 3 h. Removal of the solvent and flash chromatography of the residue gave the title chromenequinone monoacetal as a pale yellow *oil* (0.670 g, 86%) which decomposed on attempted distillation under reduced pressure; ν_{max}(film) 1 684, 1 637 and 1 605 cm^{-1}; $\delta_H(CDCl_3)$ 1.43 (6 H, s),

3.28 (6 H, s), 5.32 (1 H, d, *J* 10.0 Hz, 3-H), 6.25 (1 H, d, *J* 10.4 Hz, 6-H), 6.32 (1 H, d, *J* 10.0 Hz, 4-H), and 6.46 (1 H, d, *J* 10.4 Hz, 7-H); $\delta_C(CDCl_3)$ 28.7, 51.4, 80.6, 93.4, 111.9, 114.7, 125.3, 131.1, 140.1, 162.1 and 182.2 (Found: M^+, 236.1120. $C_{13}H_{16}O_4$ requires *M*, 236.1049).

A solution of this chromene monoacetal (0.193 g, 0.81 mmol) in tetrahydrofuran (4 ml) was cooled in an ice-bath. Cold aqueous 2M sulphuric acid was added dropwise and the solution allowed to warm to ambient temperature overnight whilst protected from light. Most of the solvent was removed at *ca.* 0.5 mmHg and the residual red oil was quickly taken into ethyl acetate and the aqueous layer removed. The organic solution was washed with brine, dried (Na_2SO_4), and evaporated. Flash chromatography of the residue (20% ethyl acetate–light petroleum as eluant) gave the previously described chromenequinone (**3**) (0.100 g, 0.52 mmol, 64%). The use of hydrochloric acid led to a chlorophenol after addition to the monoacetal.

Hydrolysis of the Quinone Ether Monoacetal (**12**).—Hydrolysis of the uncyclised monoacetal (**12**) was carried out as above to give the quinone ether (**7**) and a small quantity of chromenequinone (**3**) (*ca.* 5%). If carried out at room temperature more chromenequinone was formed (45%).

2,2-*Dimethylchromene*-6,7-*quinone* (**14**).—The 7-hydroxychromene (**6**) (0.400 g, 2.26 mmol) was added to an ice cooled solution of Frémy's salt (1.82 g, 6.82 mmol) in a mixture of water (60 ml) and methanol (8 ml) containing 1M aqueous sodium acetate (3 ml) and the mixture stirred for 3 h. The solution was extracted with ethyl acetate and the extract dried (Na_2SO_4) and evaporated. Flash chromatography of the residue (ether as eluant) gave a bright red solid (0.189 g, 0.99 mmol, 45%) obtained as red *needles*, m.p. 145–149 °C (decomp.) (from ether), ν_{max}(KBr) 1 674, 1 641 and 1 610 cm^{-1}; λ_{max}(EtOH) 240 (ε 17 700 $dm^3\ mol^{-1}\ cm^{-1}$) 339 (8 150) and 450 nm (700); $\delta_H(CDCl_3)$ 1.50 (6 H, s), 5.92 (1 H, s, 8-H), 6.15 (1 H, s, 5-H) and 6.47 (4-H) and 6.49 (3-H) (together 2 H, ABq, *J* 10.4 Hz) (irradiation of the signal at δ 1.5 led to nuclear Overhauser enhancements of 8.3, 0.0, 5.6 and 10.4% for the signals at δ 5.92, 6.15, 6.47 and 6.49 respectively); $\delta_C(CDCl_3)$ 28.5, 80.2, 108.3, 120.8, 123.4, 135.3, 143.6, 164.0, 179.1 and 181.2 (Found: C, 69.65; H, 5.4%; M^+, 190.0639. $C_{11}H_{10}O_3$ requires C, 69.45; H, 5.3%; *M*, 190.0630).

Quinoxaline of the Chromene-6,7-*quinone*.—*ortho*-Phenylenediamine (0.046 g, 0.43 mmol) was dissolved in acetic acid (4 ml) containing a few drops of ethanol. The quinone (**14**) (0.081 g, 0.43 mmol) in a little ethanol was slowly added, the reaction mixture rapidly turning very dark. When all the quinone was consumed (TLC) the solution was taken into water and extracted with ethyl acetate. The organic phase was washed with brine, dried (Na_2SO_4), and evaporated. Flash chromatography of the residue (15% ethyl acetate–light petroleum as eluant) gave the fluorescent quinoxaline in poor yield (0.030 g, 1.03 mmol, 25%); ν_{max}(KBr) 1 645, 1 455 and 1 155 cm^{-1}; $\delta_H(CDCl_3)$ 1.56 (6 H, s), 6.09 (1 H, d, *J* 10.0 Hz, 3-H), 6.69 (1 H, d, *J* 10.0 Hz, 4-H), 7.43 (1 H, s), 7.72 (1 H, dt, *J* 1.8 and 8.2 Hz), 7.76 (1 H, dt, *J* 1.8 and 10.4 Hz), 7.77 (1 H, s) and 8.14 (2 H, dd, *J* 8 and 2 Hz) (Found: M^+, 262.1121. $C_{17}H_{14}N_2O$ requires *M*, 262.1106).

4-(2-*Methylbut*-3-*yn*-2-*yloxy*)*phenol* (**17**).—A mixture of hydroquinone (3.0 g, 27.3 mmol), anhydrous potassium carbonate (4.52 g, 32.7 mmol), potassium iodide (7.2 g, 44 mmol), and 3-chloro-3-methylbutyne in dry acetone (45 ml) was heated under reflux in an atmosphere of nitrogen for 24 h. Solvent was then evaporated and the residue partitioned between ethyl acetate and dilute hydrochloric acid. The organic layer was washed with brine, dried (Na_2SO_4), and evaporated. Flash chromatography of the residue (20% ethyl acetate–light petroleum as eluant) gave the monoalkylated product (1.58 g, 9.0 mmol, 33%) as colourless hexagonal *plates*, m.p. 132–134 °C (from chloroform); ν_{max}(KBr) 3 300br, 3 270, 2 110 and 1 510 cm^{-1}; $\delta_H(CDCl_3)$ 1.54 (6 H, s), 3.02 (1 H, s), 6.75 (2 H, d, *J* 9 Hz) and 7.03 (1 H, d, *J* 9 Hz); $\delta_C(CDCl_3)$ 30.2, 73.6, 75.3, 87.6, 116.2, 124.8, 149.3 and 154.6 (Found: M^+, 176.0826. $C_{11}H_{12}O_2$ requires *M*, 176.0837).

2,2-*Dimethylchromen*-6-*ol* (**16**).—The ether (**17**) (0.360 g, 2.0 mmol) in degassed *o*-xylene (50 ml) was boiled under reflux overnight in an atmosphere of nitrogen. Solvent was evaporated and the residue subjected to flash chromatography (15% ethyl acetate–light petroleum as eluant) to give the title chromenol (0.328 g, 91%), m.p. 92–93 °C (from dichloromethane–light petroleum) (lit.,[30] NMR data only), ν_{max}(KBr) 3 405, 1 615, 1 595, 1 505 and 1 210 cm^{-1}; $\delta_H(CDCl_3)$ 1.41 (6 H, s), 5.62 (1 H, d, *J* 9.8 Hz, 3-H), 6.20 (1 H, d, *J* 9.8 Hz, 4-H), 6.51 (1 H, d, *J* 2.8 Hz, 5-H), 6.60 (1 H, dd, *J* 8.6 and 2.8 Hz, 6-H) and 6.67 (1 H, d, *J* 8.6 Hz, 8-H) (the addition of a drop of deuteriated trifluoroacetic acid caused the appearance of a signal at δ 9.5); $\delta_C(CDCl_3)$ 27.6, 76.1, 113.2, 115.7, 117.6, 122.27, 122.30, 131.9 and 146.6 (Found: C, 75.1; H, 6.95%; M^+, 176. Calc. for $C_{11}H_{12}O_2$: C, 75.0; H, 6.9%; *M*, 176).

Frémy Oxidation of 2,2-*Dimethylchromen*-6-*ol*.—The chromen-6-ol (**16**) (2.0 g, 11.4 mmol) in acetone (50 ml) was added over 0.5 h to an ice-cooled solution of Frémy's salt (6.2 g, 23.3 mmol) in water (600 ml), acetone (175 ml), and 0.167M aqueous potassium dihydrogen phosphate (99 ml). The cold solution was stirred for 2 h and extracted with ethyl acetate. The organic phase was dried (Na_2SO_4) and evaporated in the cold. Flash chromatography of the residue (30–50% ethyl acetate–light petroleum as eluant) gave the previously described chromenequinone (**14**) (1.47 g, 7.74 mmol, 68%).

4-(2-*Methylbut*-3-*yn*-2-*yloxy*)-1,2-*benzoquinone* (**18**).—The ether (**17**) (0.397 g, 2.31 mmol) in acetone (5 ml) was added to an ice-cooled solution of Frémy's salt (1.30 g, 4.84 mmol) in water (123 ml), acetone (38 ml), and 0.167M aqueous potassium dihydrogen phosphate (21 ml). After 3 h the solution was extracted with ethyl acetate (3 × 30 ml) and the extract washed with brine, dried (Na_2SO_4), and evaporated to give the red crystalline title *o-quinone ether* (0.317 g, 80%) which appeared homogeneous (TLC) but could not be recrystallised; ν_{max}(KBr) 3 290, 2 110 and 1 650br cm^{-1}; $\delta_H(CDCl_3)$ 1.73 (6 H, s), 2.80 (1 H, s), 6.17 (1 H, d, *J* 2.8 Hz, 3-H), 6.28 (1 H, d, *J* 10.5 Hz, 6-H), and 6.73 (1 H, dd, *J* 10.5 and 2.8 Hz, 5-H) (Found: M^+, 190.0655. $C_{11}H_{10}O_3$ requires *M*, 190.0630).

Cyclisation of the o-*Quinone Ether* (**18**).—The ether (**18**) (0.060 g, 0.32 mmol) in acetone (100 ml) was heated at 35 °C overnight whereupon TLC showed complete conversion into the chromene-*p*-quinone (**3**). Flash chromatography (30% ethyl acetate–light petroleum as eluant) gave the chromene (**3**) as the sole product (0.058 g, 97%).

6,7-*Dimethoxy*-2,2-*dimethylchroman*-4-*one* (**23**).—This starting material was obtained on a large scale by Baeyer–Villiger oxidation of veratraldehyde (using a suspension of 3-chloroperoxybenzoic acid in dichloromethane over 2 days), hydrolysis of the resultant formate ester to 3,4-dimethoxyphenol, and chromanone formation using 3,3-dimethylacrylic acid and phosphorus pentoxide in methanesulphonic acid,[36] to give colourless needles, m.p. 106 °C (from light petroleum) (lit.,[37] 106 °C); $\delta_C(CDCl_3)$ 26.6 (q), 48.3 (t), 56.10 and 56.11 (both q), 79.5 (s), 100.5 (d) (8-C), 106.4 (d) (5-C), 112.3 (s), (4a-C) 144.0 (s) (6-C), 156.27 (s), 156.29 (s) and 190.7 (s). 3,4-Dimethoxyphenol

is available commercially but is considerably more expensive than material produced as indicated.

6,7-*Dimethoxy*-2,2-*dimethyl*-3-*nitrochroman*-4-*one*.—A solution of 6,7-dimethoxy-2,2-dimethylchroman-4-one (**23**) (0.5 g, 2.1 mmol) in trifluoroacetic anhydride (6 ml) at 0 °C was treated with finely ground ammonium nitrate (178 g, 2.2 mmol) and the mixture maintained at that temperature until all starting material had disappeared (2 h). The solution was evaporated and the residue dissolved in dichloromethane (5 ml) and the solution passed through a silica gel column. Removal of the solvent from the eluant left a yellow solid which gave the title 3-nitrochromanone (0.175 g, 30%) as pale yellow *needles*, m.p. 141–143 °C (from ethyl acetate–light petroleum); ν_{max}(KBr) 1 692, 1 612, 1 565 and 1 503 cm^{-1}; λ_{max}(EtOH) 210 (end abs.) (ε 13 600 dm^3 mol^{-1} cm^{-1}), 241 (11 800), 283 (9 950) and 351 nm (14 550); $\delta_H(CDCl_3)$ 1.45 and 1.51 (each 3 H, s, C-Me_2), 3.75 and 3.80 (each 3 H, s, OMe), 5.03 (1 H, s, 3-H), 6.30 (1 H, s, 8-H) and 7.10 (1 H, s, 5-H); $\delta_C(CDCl_3)$ 23.1 and 24.8 (both q), 56.3 and 56.5 (both q), 80.2 (s), 92.9 (d), 100.8 (d), 106.8 (d), 110.9 (s), 145.3 (s), 156.1 (s), 157.9 (s) and 179.3 (s) (Found: C, 55.3; H, 5.35; N, 4.9%; M^+, 281.0913. $C_{13}H_{15}NO_6$ requires C, 55.5; H, 5.4; N, 5.0%; *M*, 281.0899).

3,3-*Dibromo*-6,7-*dimethoxy*-2,2-*dimethylchroman*-4-*one*.—The chromanone (**23**) (20 g, 84.7 mmol) was dissolved in a dry mixture of chloroform and ethyl acetate (500 ml, 1:1) and to this was added cupric bromide (85 g, 381 mmol). The mixture was boiled under reflux with vigorous stirring until TLC showed the absence of the monobromo product first formed (*ca.* 3 days). The solid was filtered off and washed with ethyl acetate (2 × 100 ml). The combined organic layers were washed with water (2 × 100 ml) and brine (1 × 100 ml), dried ($MgSO_4$). Removal of the solvent, after filtration through a silica gel column, gave the title dibromochromanone (98%), as pale yellow *prisms*, m.p. 108–109 °C (from chloroform–light petroleum); ν_{max}(KBr) 1 686, 1 613 and 1 505 cm^{-1}; λ_{max}(EtOH) 207 (end abs.) (ε 12 900 dm^3 mol^{-1} cm^{-1}) 239 (8 250), 285 (6 100) and 352 nm (4 300); $\delta_H(CDCl_3)$ 1.85 (6 H, s), 3.96 and 4.00 (each 3 H, s), 6.51 (1 H, s, 8-H) and 7.40 (1 H, s, 5-H); $\delta_C(CDCl_3)$ 20.19 and 26.33 (each above a broad background indicative of slow ring-flipping on the NMR timescale), 56.2, 56.3, 75.4, 85.7, 100.3, 107.6, 108.0, 145.1, 153.9, 157.1 and 179.1 (Found: C, 39.75; H, 3.4%; M^+, 391.9234. $C_{13}H_{14}Br_2O_4$ requires C, 39.6; H, 3.6%; *M*, 391.9258).

3-*Bromo*-6,7-*dimethoxy*-2,2-*dimethylchroman*-4-*one*.—Repetition of the above preparation with either the addition of half the quantity of cupric bromide or work-up of the reaction when TLC showed only the first product to be present, gave the title monobromochromanone (99%) as pale yellow *prisms*, m.p. 152–153 °C (from light petroleum–ethyl acetate); ν_{max}(KBr) 1 674 and 1 616 cm^{-1}; λ_{max}(EtOH) 208 (end abs.) (ε 14 500 dm^3 mol^{-1} cm^{-1}), 236 (15 400), 283 (10 900), and 350 nm (7 800); $\delta_H(CDCl_3)$ 1.50 (3 H, s), 1.60 (3 H, s), 3.83 (3 H, s), 3.85 (3 H, s), 4.25 (1 H, s, 3-H), 6.37 (1 H, s, 8-H) and 7.20 (1 H, s, 5-H); $\delta_C(CDCl_3)$ 22.9 and 26.2, 56.1, 56.2 and 56.3, 80.3, 100.4, 107.2, 109.7, 144.8, 155.2, 157.0 and 185.1 (Found: C, 49.6; H, 4.65%; M^+, 314.0140. $C_{13}H_{15}BrO_4$ requires C, 49.5; H, 4.8%; *M*, 314.0154).

3,3-*Dibromo*-6,7-*dimethoxy*-2,2-*dimethyl*-5-*nitrochroman*-4-*one* (**24**).—To a solution of the dibromochromanone (**7**) (30 g, 75.9 mmol) in acetic anhydride (300 ml) was added anhydrous cupric acetate (4.5 g, 25 mmol). The mixture was stirred and heated to 90 °C for 15 min. After the mixture had cooled to 60 °C finely ground cupric nitrate trihydrate (21.9 g, 90.9 mmol) was carefully added in portions to the mixture so as to keep the temperature < 65 °C. The mixture was stirred at 60 °C for a further 4 h and then poured into water (100 ml) and the mixture stirred overnight. Extraction with ethyl acetate (4 × 100 ml) and removal of the dried ($MgSO_4$) solvent gave an oil which on silica-gel chromatography yielded first (ether as eluant) any starting material and then (ethyl acetate as eluant) the 5-nitro derivative (13.46 g, 45%) which was obtained as pale yellow *needles*, m.p. 143–144 °C (from light petroleum–dichloromethane); ν_{max}(KBr) 1 701, 1 620, 1 548 and 1 499 cm^{-1}; λ_{max}(EtOH) 210 (end abs.) (ε 20 000 dm^3 mol^{-1} cm^{-1}), 229sh (12 700), 283 (8 800) and 333 nm (6 100); $\delta_H(CDCl_3)$ 1.90 (6 H, s), 3.95 (3 H, s), 4.16 (3 H, s) and 6.67 (1 H, m, 8-H); $\delta_C(CDCl_3)$ 23.1 (q), 56.9 (q), 62.5 (q), 73.0 (s), 86.5 (s), 100.0 (s), 102.1 (d), 137.0 (s), 145.1 (s), 153.9 (s), 160.6 and 175.9 (s) (Found: C, 35.55; H, 3.0%; M^+ 436.9201. $C_{13}H_{13}Br_2NO_6$ requires C, 35.6; H, 33.0%; *M*, 436.9108).

5-*Amino*-6,7-*dimethoxy*-2,2-*dimethylchroman*-4-*one* (**25**).—To a solution of the 5-nitrochromanone (**24**) (21 g, 47.8 mmol) in ether (800 ml) was added water (12 ml), acetic acid (20 ml), and zinc dust (9.7 g, 150 mmol). The mixture was stirred vigorously at room temperature overnight. The solids (zinc and zinc salts) were filtered off and washed with ether (3 × 50 ml). The combined organic solutions were washed with saturated aqueous sodium hydrogen carbonate (2 × 100 ml) and brine (100 ml), dried ($MgSO_4$), and evaporated to leave a light brown oil which afforded the aminochromanone (**25**) (10.6 g, 88%) as colourless *needles*, m.p. 93–94 °C (from light petroleum); ν_{max}(KBr) 3 399, 3 298, 1 636 and 1 610 cm^{-1}; λ_{max}(EtOH) 210sh (end abs.) (ε 25 100 dm^3 mol^{-1} cm^{-1}), 224 (34 600), 245sh (16 700), 293 (20 100) and 358 nm (5 500); $\delta_H(CDCl_3)$ 1.55 (6 H, s), 2.75 (2 H, s, 3-H_2), 3.90 and 4.00 (each 3 H, s), 5.25 (2 H, br s) and 5.95 (1 H, s, 8-H) (treatment with D_2O caused the signal at δ 5.25 to disappear); $\delta_C(CDCl_3)$ 26.7 (q), 49.0 (t), 55.7 (q), 59.8 (q), 78.1 (s), 88.8 (d), 101.0 (s), 127.9 (s), 144.3 (s), 158.1 (s), 158.1 (s) and 193.1 (Found: C, 61.95; H, 6.65; N, 5.4%; M^+, 251.1067. $C_{13}H_{17}NO_4$ requires C, 62.1; H, 6.8; N, 5.6%; *M*, 251.1157).

6,7-*Dimethoxy*-2,2-*dimethyl*-4-*oxochroman*-5,8-*quinone* (**26**).—A solution of the aminochromanone (**25**) (20 g, 7.9 mmol) in acetone (50 ml) was added over 15 min to a solution of Frémy's salt (6.4 g, 23.9 mmol) in water (350 ml) and the mixture was then stirred at room temperature until the purple colour of the reagent had disappeared (1 h). The solution was extracted with ethyl acetate (4 × 150 ml) and the combined extracts were washed with brine (100 ml), dried ($MgSO_4$), and evaporated to yield the title quinone (17.0 g, 80%) as orange *needles*, m.p. 120–121 °C (from ethyl acetate–light petroleum); ν_{max}(KBr) 1 713, 1 663, and 1 618 cm^{-1}; λ_{max}(EtOH) 207 (end abs.) (ε 8 000 dm^3 mol^{-1} cm^{-1}), 257 (8 650) and 301 nm (12 850); $\delta_H(CDCl_3)$ 1.55 (6 H, s), 2.52 (2 H, s) and 3.89 and 4.05 (each 3 H, s); $\delta_C(CDCl_3)$ 26.0 (q), 48.3 (t), 61.2 (q), 61.5 (q), 85.0 (s), 109.1 (s), 143.6 (s), 145.8 (s), 160.5 (s), 178.2 (s), 178.5 (s) and 188.0 (s) (Found: C, 58.6; H, 5.2%; M^+, 266.0793. $C_{13}H_{14}O_6$ requires C, 58.7; H, 5.4%; *M*, 266.0790).

6,7-*Dimethoxy*-2,2-*dimethyl*-4-*oxochroman*-5,8-*quinone* 5-*Imine*.—Chromatography (1% methanol in ether) of the mother liquors of the above Frémy oxidation afforded the title imine (0.600 g, 3%) as bright orange *needles*, m.p. 200–201 °C (from light petroleum–ethyl acetate); ν_{max}(KBr) 3 494, 3 285, 1 674, 1 624, 1 587 and 1 516 cm^{-1}; λ_{max}(EtOH) 205 (end abs.) (ε 9 800 dm^3 mol^{-1} cm^{-1}), and 292 nm (15 600); $\delta_H(CDCl_3)$ 1.35 (6 H, s), 3.15 (2 H, s), 3.95 (3 H, s), 4.00 (3 H, s) and 7.6 (1 H, br s) (treatment with D_2O caused the signal at δ 7.6 to disappear); $\delta_C(CDCl_3)$ 29.9 (q), 53.0 (t), 61.1 (q), 62.3 (q), 70.9 (s), 105.6 (s), 142.4 (s), 145.1 (s), 161.6 (s), 174.5 (s), 179.0 (s) and 202.5 (s) (Found: C, 58.7; H, 5.8; N, 5.4%; $M^+ + 2$, 267.1114.

$C_{13}H_{15}NO_5$ requires C, 58.9; H, 5.7; N, 5.3%; M + 2, 267.1107).

5,8-*Dihydroxy*-6,7-*dimethoxy*-2,2-*dimethylchroman*-4-*one* (**27**).—A solution of the chromanone (**26**) (0.133 g, 0.5 mmol) in acetone (20 ml) was stirred with aqueous sodium bisulphite (0.5M; 20 ml). The mixture was diluted with ethyl acetate (30 ml), the organic phase dried ($MgSO_4$), and the solvent removed. The residue afforded the title hydroquinone as pale yellow *needles* (0.130 g, 98%), m.p. 135–136 °C (from ethyl acetate–light petroleum); ν_{max}(KBr) 3 413br, 1 645 and 1 621 cm^{-1}; λ_{max}(EtOH) 214 (ε 9 600 dm^3 mol^{-1} cm^{-1}), 240sh (2 900), 294 (6 600) and 392 nm (1 450); δ_H($CDCl_3$) 1.45 (1 H, s), 2.65 (2 H, s), 3.80 and 4.05 (each 3 H, s) (addition of CF_3CO_2D caused the appearance of a new singlet at δ 9.3 integrating for 2 H); δ_C($CDCl_3$) 26.7 (q), 48.4 (t), 61.1 (q), 61.3 (q), 79.8 (s), 103.4 (s), 129.8 (s), 133.4 (s), 141.9 (s), 148.6 (s), 149.0 (s) and 197.1 (s) (Found: C, 58.25; H, 6.0%; M^+, 268.0950. $C_{13}H_{16}O_6$ requires C, 58.2; H, 6.0% M, 268.0947).

5,8-*Diacetoxy*-6,7-*dimethoxy*-2,2-*dimethylchroman*-4-*one* (**28**).—The above hydroquinone (**27**) (0.080 g, 0.3 mmol) in acetic anhydride (5 ml) was treated with concentrated sulphuric acid (1 drop) and left overnight at room temperature. The mixture was poured into water (10 ml) and stirred for 1 h. The mixture was extracted with ethyl acetate (3 × 25 ml) and the combined extracts were washed with saturated aqueous sodium hydrogen carbonate (3 × 25 ml) and brine (25 ml), dried ($MgSO_4$), and evaporated to leave a colourless oil which afforded the title diacetate as colourless *needles* (0.100 g, 95%), m.p. 92–93 °C (from ethyl acetate–light petroleum); ν_{max}(KBr) 1 771, 1 687 and 1 612 cm^{-1}; λ_{max}(EtOH) 222 (ε 45 500 dm^3 mol^{-1} cm^{-1}), 268 (23 800) and 329 nm (8 400); δ_H($CDCl_3$) 1.40 (6 H, s), 2.30 and 2.40 (each 3 H, s, OAc), 2.60 (2 H, s), 3.80 and 3.95 (each 3 H, s); δ_C($CDCl_3$) 20.3 (q), 20.9 (q), 26.4 (q), 49.8 (t), 61.3 (q), 61.7 (q), 80.3 (s), 109.6 (s), 130.7 (s), 139.6 (s), 141.1 (s), 149.7 (s), 152.4 (s), 168.2 (s), 169.1 (s) and 189.5 (s) (Found: C, 57.95; H, 5.85%; M^+, 352.1140. $C_{17}H_{20}O_8$ requires C, 57.95; H, 5.7%; M, 352.1158).

8-*Acetoxy*-6,7-*dimethoxy*-2,2-*dimethylchroman*-5-*ol* (**29**).—To a solution of the diacetate (**28**) (0.055 g, 0.156 mmol) in tetrahydrofuran (5 ml) was added sodium borohydride (0.006 g, 0.156 mmol). The mixture was stirred for 30 min and the solvent was then removed by evaporation. The residue was dissolved in ethyl acetate (10 ml) and the solution washed with water (10 ml) and brine (10 ml), dried ($MgSO_4$) and evaporated to give the title chroman as a colourless *oil* (0.037 g, 80%); ν_{max}(KBr) 3 500br, and 1 704 cm^{-1}; δ($CDCl_3$) 1.20 (6 H, s), 1.65 (2 H, t, J 6 Hz, 3-CH_2), 2.20 (3 H, s, OAc), 2.55 (2 H, dd, J 6 Hz, 4-CH_2) and 3.75 (6 H, s) [additional of D_2O caused the appearance of a signal (1 H) at δ 4.6] (Found: M^+, 296.1259. $C_{15}H_{20}O_6$ requires M, 296.1259).

The same product was obtained, together with starting material, when only 1.5 mg (1 equiv.) of sodium borohydride was used.

4-*Hydroxy*-6,7-*dimethoxy*-2,2-*dimethylchroman*-5,8-*quinone* (**30**).—Sodium borohydride reduction of the quinonoid chromanone (**26**) (0.410 g, 1.54 mmol) was carried out as above and the residue obtained on removal of the tetrahydrofuran dissolved in dichloromethane and shaken with aqueous ferric chloride (1M; 5 ml). Alternatively, the solution could be left overnight or boiled under reflux for 10 min. The dark red solution was filtered through a little alumina and the solvent removed to leave an orange *oil*; ν_{max}(KBr) 3 518, 1 673, 1 643 and 1 603 cm^{-1}; λ_{max}(EtOH) 209 (end abs.) (13 900 dm^3 mol^{-1} cm^{-1}) and 298 nm (11 200); δ_H($CDCl_3$) 1.41 (3 H, s), 1.51 (3 H, s), 1.95 (1 H, *A*BX m, J_{AB} 14.5 Hz, 3-H_a), 2.04 (1 H, A*B*X m, 3-H_b), 3.40 (1 H, br), 3.94 (3 H, s), 4.09 (3 H, s, 4-H) and 4.80 (1 H, AB*X* dd) (on treatment with D_2O the signal at δ 3.40 disappeared); δ_C($CDCl_3$) 26.9 (q) (two accidentally co-incident signals), 39.7 (t), 59.5 (d), 61.4 (q), 61.5 (q), 80.2 (s), 115.6 (s), 142.7 (s), 145.6 (s), 151.1 (s), 179.1 (s) and 184.6 (s) (Found: M^+ 268.0950. $C_{13}H_{16}O_6$ requires M, 268.0947).

Acetylation of the alcohol (**30**) gave the acetate (**31**), as a deep orange *oil*; ν_{max}(KBr) 1 748, 1 673, 1 648 and 1 605 cm^{-1}; δ_H($CDCl_3$) 1.46 and 1.50 (each 3 H, s), 2.00–2.28 (2 H, *AB*X m, 3-H_2), 2.05 (3 H, s), 3.94 and 4.10 (each 3 H, s) and 5.88 (1 H, dd, J_{AX} 3 Hz, J_{BX} 5 Hz, 4-H); δ_C($CDCl_3$) 21.0 (q), 25.4 (q), 28.7 (q), 38.3 (t), 60.3 (d), 61.3 (q), 61.4 (q), 79.3 (s), 111.9 (s), 142.9 (s), 146.0 (s), 153.1 (s), 170.0 (s), 178.7 (s) and 181.43 (Found: M^+, 310.1030. $C_{15}H_{16}O_7$ requires M, 310.1052).

5,8-*Diacetoxy*-6,7-*dimethoxy*-2,2-*dimethylchroman*-4-*yl Acetate* (**32**).—The chromanone (**26**) (0.110 g, 0.42 mmol) in tetrahydrofuran (15 ml) was stirred with sodium borohydride (0.008 g, 0.22 mmol) for 1 h. Removal of the solvent left a yellow residue which, on dissolution in ethyl acetate, rapidly turned orange (atmospheric oxidation to the quinonoid chromanol). On repetition of the reduction the residue (still containing a slight excess of sodium borohydride) was dissolved in dry pyridine (6 ml). The solution was treated with acetic anhydride (13.3 g, 1.3 mmol) and a trace of 4-dimethylaminopyridine and left overnight at room temperature. The mixture was poured into water (30 ml), the mixture stirred for 2 h and then extracted with ethyl acetate (4 × 10 ml). The combined extracts were washed with aqueous sulphuric acid (1M; 2 × 5 ml), water (10 ml), and saturated aqueous sodium hydrogen carbonate (3 × 5 ml), dried ($MgSO_4$), and evaporated to leave an oil which on silica-gel chromatography (dichloromethane as solvent) afforded the title triacetate as colourless *needles* (0.148 g, 57%), m.p. > 220 °C (sublimes) (from ethyl acetate–light petroleum); ν_{max}(KBr) 1 773 and 1 738 cm^{-1}; δ_H($CDCl_3$) 1.38 (6 H, s), 2.00 and 2.08 (together 2 H, *AB*X ddd, J_{AB} 15 Hz, J_{AX} 3.1 Hz, J_{BX} 5.2 Hz, 3-H_2), 2.04, 2.26, 2.34 (each 3 H, s, OAc), 3.80, 3.88 (each 3 H, s) and 6.00 (1 H, AB*X* dd, J 3.1 and 5.2 Hz, 4-H); δ_C($CDCl_3$) 20.4, 20.46, 21.1, 25.66, 29.0, 39.1, 61.1, 61.2, 61.9, 75.1, 109.1, 131.4, 138.9, 140.9, 143.5, 147.6, 168.5, 168.5 and 170.2 (Found: M^+, 396.141 9. $C_{19}H_{24}O_9$ requires M, 396.1420).

6,7-*Dimethoxy*-2,2-*dimethylchromene*-5,8-*quinone* (**22**).—A solution of the quinonoid chromanol (**30**) (0.190 g, 0.70 mmol) in dry benzene (10 ml) containing a little toluene-*p*-sulphonic acid was boiled under reflux until TLC showed that all starting material had disappeared (45 min). After it had cooled the solution was passed through a short column of alumina. Removal of the solvent from the eluant afforded the title chromenequinone (**22**) as dark red *needles* (0.140 g, 80%), m.p. 89–90 °C (from light petroleum); ν_{max}(KBr) 1 723 and 1 650 cm^{-1}; λ_{max}(EtOH) 213 (ε 12 500 dm^3 mol^{-1} cm^{-1}), 258 (7 400), 285sh (4 700), and 323 nm (8 100); δ_H($CDCl_3$) 1.43 (6 H, s), 3.88 (3 H, s), 3.99 (3 H, s), 5.50 (1 H, d, J 10 Hz, 3-H) and 6.35 (1 H, d, J 10 Hz, 4-H); δ_C($CDCl_3$) 28.3 (q), 61.3 (q), 81.0 (s), 113.4 (s), 114.7 (d), 129.4 (d), 143.2 (s), 144.8 (s), 149.5 (s), 178.7 (s) and 180.6 (s) (Found: C, 62.5; H, 5.75%; M^+ 250.0849. $C_{13}H_{14}O_5$ requires C, 62.4; H, 5.6%; M, 250.0841).

3,4,5-*Trimethoxyphenyl* 2-*Methylbut*-3-*yn*-2-*yl Ether* (**34**).—A mixture of 3,4,5-trimethoxyphenol (3.9 g, 21 mmol), 3-chloro-3-methylbutyne (3.24 g, 32 mmol), anhydrous potassium carbonate (4.32 g, 32 mmol), and dry acetone (150 ml) was boiled under reflux until all the phenol had reacted (TLC, 36 h). The bulk of the solvent was evaporated and the residue treated with water (25 ml). The mixture was extracted with dichloromethane (3 × 15 ml) and the combined extracts were

washed with aqueous sodium hydroxide (2M; 35 ml), water (25 ml) and brine (25 ml) and dried ($MgSO_4$). Removal of the solvent left a residue which was chromatographed on silica gel (dichloromethane–ether as eluant). The first fraction consisted of the title ether (1.86 g, 35%) which gave colourless *prisms*, m.p. 72–73 °C (from light petroleum–ether); ν_{max}(KBr) 3 278, 2 085, 1 596 and 1 502 cm^{-1}; λ_{max}(EtOH) 209 (end abs.) (ε 14 000 dm^3 mol^{-1} cm^{-1}), 230sh (3 100) and 273 nm (500); $\delta_H(CDCl_3)$ 1.60 (6 H, s), 2.59 (1 H, s), 3.72 (9 H, s) and 6.45 (2 H, s); $\delta_C(CDCl_3)$ 29.6, 56.1, 61.0, 72.7, 73.7, 86.6, 99.5, 134.2, 151.8 and 153.1 (Found: C, 67.3; H, 7.1%; M^+, 250.1172. $C_{14}H_{18}O_4$ requires C, 67.2; H, 7.25%; *M*, 250.1205).

3,4,5-*Trimethoxy*-4-(2-*methylbut*-3-*yn*-2-*yl*)*cyclohexa*-2,5-*dienone* (**35**).—The second fraction from the above alkylation was the title cyclohexadienone (1.85 g, 35%), obtained as colourless *needles*, m.p. 151–152 °C (from ether–light petroleum); ν_{max}(KBr) 3 238, 1 657, 1 619 and 1 588 cm^{-1}; λ_{max}(EtOH) 207 (end abs.) (ε 3 600 dm^3 mol^{-1} cm^{-1}), 248 (10 300) and 298 nm (2 200); $\delta_H(CDCl_3)$ 1.32 (6 H, s), 2.15 (1 H, s), 3.15 (3 H, s), 3.71 (6 H, s) and 5.57 (2 H, s); $\delta_C(CDCl_3)$ 26.5 (q), 41.6 (s), 54.3 (q), 55.6 (q), 70.7 (d), 83.9 (s), 88.4 (d) (long-range coupling, *J* 50 Hz), 105.1 (d), 170.1 (s) and 187.3 (s) (Found: C, 67.35; H, 7.2%; M^+, 250.1222. $C_{14}H_{18}O_4$ requires C, 67.12; H, 7.25%; *M*, 250.1205).

3,5-*Dimethoxy*-4-*nitrophenol*.—The phenolic ether (**34**) (0.150 g, 0.6 mmol) was dissolved in trifluoroacetic anhydride and the solution cooled to −5 °C. To the solution was added ammonium nitrate (0.048 g, 0.6 mmol) over 1 h. The mixture was stirred for a further 2 h and kept at −10 °C overnight. The solvent was removed, the residue dissolved in dichloromethane (5 ml), and the solution passed through a little alumina. After being concentrated the eluant was subjected to silica-gel chromatography (1% methanol in dichloromethane as eluant). The only significant material isolated was the title phenol (0.050 g, 42%), m.p. 165–166 °C (from light petroleum–ether) (lit.,[38] 165–166 °C); ν_{max}(KBr) 3 404, 1 645, 1 598 and 1 112 cm^{-1}; λ_{max}(EtOH) 208 (end abs.) (ε 2 300 dm^3 mol^{-1} cm^{-1}), 235 sh (1 200) and 285 nm (4 000); $\delta(CDCl_3)$ 3.70 (6 H, s) and 5.72 (2 H, s) [the addition of [^{1}H]trifluoroacetic acid caused a signal at δ 9.2 (1 H, s) to appear] (Found: C, 48.4; H, 4.6; N, 7.15%; M^+, 199. Calc. for $C_8H_9NO_5$: C, 48.25; N, 7.1%; *M*, 199).

3,4-*Epoxy*-2,2-*dimethylchromene*-5,8-*quinone*.—3-Chloroperbenzoic acid (1.80 g, 10.6 mmol) in dichloromethane previously stored over basic alumina; 20 ml) was added slowly to a stirred mixture of the chromene-5,8-quinone (**3**) (0.503 g, 2.65 mmol) and potassium carbonate (0.73 g, 5.3 mmol) in dichloromethane (stored as before; 30 ml). The mixture was stirred at room temperature for 8 h and the solution then filtered and the solvent evaporated. Flash chromatography (30% ethyl acetate–light petroleum) gave the title epoxide (0.072 g, 0.35 mmol, 13%) and starting material (0.120 g). The epoxide was sublimed (120 °C/0.1 mmHg) to give yellow *needles*, m.p. 110–111 °C; ν_{max}(KBr) 1 672, 1 674 and 1 574 cm^{-1}; λ_{max}(cyclohexane) 252 (ε 1 400 dm^3 mol^{-1} cm^{-1}), 295sh (1 750) and 377 nm (1 850); $\delta_H(CDCl_3)$ 1.42 (3 H, s), 1.66 (3 H, s), 3.50 (1 H, d, *J* 4.4 Hz, 3-H), 4.13 (1 H, d, 4.4 Hz, 4-H) and 6.72 (2 H, ABq, Δδ 0.05 ppm, *J* 10.2 Hz, 6- and 7-H) (Found: M^+, 206.0576. $C_{11}H_{10}O_4$ requires *M*, 206.0579).

A large excess of peracid was essential to ensure that the rate of formation of the slower running epoxide was sufficient. However, the reaction could not be allowed to proceed to completion because the product reacted further.

Anhydride (**36**) *Derived from* 2,2-*Dimethylchromene*-6,7-*quinone* (**14**).—To an ice cooled stirred solution of the chromene-*o*-quinone (**14**) (0.010 g, 0.53 mmol) in dichloromethane (2 ml) was added 3-chloroperoxybenzoic acid (0.015 g, 0.087 mmol). After 3 h the red starting material had disappeared (TLC and visual). The solvent was evaporated and the residue subjected to preparative TLC (0.25 mm thickness silica) (80% ether–light petroleum as eluant) to give the title *anhydride* (0.007 g, 65%), ν_{max}(KBr) 1 777 and 1 725 cm^{-1}; $\delta_H(CDCl_3)$ 1.47 (6 H, s), 6.04 (1 H, s, original 8-H), 6.22 (1 H, d, *J* 10.1 Hz, 3-H), 6.24 (1 H, s, original 5-H) and 6.36 (1 H, d, *J* 10.1 Hz, 4-H) (Found: M^+, 206.0571. $C_{11}H_{10}O_4$ requires *M*, 206.0578).

cis- *or* trans-3,4-*Dibromo*-6,7-*dimethoxy*-2,2-*dimethylchromene*-5,8-*quinone*.—The chromenequinone (**22**) (0.061 g, 0.24 mmol) was dissolved in tetrahydrofuran (10 ml) and to the solution was added *N*-bromoacetamide (0.041 g, 0.29 mmol, 1.2 equiv.). The mixture was stirred overnight and then passed through a short column of Florisil. Evaporation of the solvent furnished a red *oil* (0.050 g, 50%), ν_{max}(film) 1670 and 1602 cm^{-1}; $\delta_H(CDCl_3)$ 1.66 (3 H, s), 1.78 (3 H, s), 3.96 (3 H, s), 4.11 (3 H, s), 4.55 (1 H, d, *J* 2.6 Hz) and 5.44 (1 H, d, *J* 2.6 Hz) (Found: M^+, 407.9206. $C_{13}H_{14}Br_2O_5$ requires *M*, 107.9208).

The same compound was formed when wet or dry tetrahydrofuran was used and when the *N*-bromoacetamide was replaced with *N*-bromosuccinimide.

3-*Bromo*-6,7-*dimethoxy*-2,2-*dimethylchromene*-5,8-*quinone*.—The above dibromide (0.050 g) was left overnight at room temperature, the red oil becoming deep purple. The oil was passed through a little alumina (dichloromethane as eluant) to give an *oil* (0.030 g, 75%), ν_{max}(film) 1 651, 1 606 and 1 208 cm^{-1}; $\delta_H(CDCl_3)$ 1.7 (6 H, s), 4.0 (3 H, s), 4.1 (3 H, s) and 6.75 (1 H, s) (Found: M^+, 327.9942. $C_{13}H_{13}BrO_5$ requires *M*, 327.9946).

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