Structural Revision and Synthesis of LL-D253α and Related Chromanone Fungal Metabolites

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The structure of LL-D253α, a chromanone metabolite of *Phoma pigmentivora* has been revised by analysis of the ^{1}H-coupled ^{13}C NMR spectrum to 7-hydroxy-8-(2′-hydroxyethyl)-5-methoxy-2-methylchroman-4-one. This has been further established by the synthesis of the revised and previously proposed structures of LL-D253α.

In 1972 three antibiotic chromanone metabolites were isolated by McGahren and co-workers from *Phoma pigmentivora*.[1] The major metabolite, designated LL-D253α was assigned structure **1**, 5-hydroxy-6-(2′-hydroxyethyl)-7-methoxy-2-methylchroman-4-one. Two minor co-metabolites, LL-D253β and LL-D253γ, were assigned structures **2** and **3** respectively. The substitution patterns of the chromanone structures **1**–**3** were assigned mainly on the basis of IR evidence. The carbonyl IR band, originally at 1655 cm^{-1} in LL-D253α, moved to 1699 cm^{-1} in the derived diacetate which indicated that the hydroxy group occupied the position *peri* to the chromanone carbonyl. This will be discussed in more detail below. On treatment with sulfuric acid a dihydrofuran formulated as **3** was formed so that the hydroxyethyl side chain must be *ortho* to the phenolic hydroxy. In addition, LL-D253α gave a positive Gibbs test,[2] which is generally taken to indicate that the ring position *para* to the phenolic hydroxy is unsubstituted. The methoxy group was, therefore, placed at C-7 on the chromanone.

LL-D253α was isolated independently by a Japanese group, also from a *Phoma* strain.[3] IR data again led to the assumption of an *ortho*-hydroxy aryl ketone structure; in this case the carbonyl band, quoted at 1640 cm^{-1}, was compared with that of the methyl ether at 1685 cm^{-1}. On the basis of nuclear Overhauser enhancements (NOE) observed in the ^{1}H NMR spectra, structure **4** with the hydroxyethyl side-chain at C-8 was initially favoured, but on publication of structure **1** by the American group both compounds were shown to be identical. LL-D253α has also been isolated from *Sclerotinia fructigena* and *Phoma violacea*; the latter species also produced LL-D253γ and another closely related compound formulated as **5** with an ethyl instead of an ethanolic side-chain.[4]

In the course of biosynthetic studies to determine the origin of the C_2 side-chain found in LL-D253α and other metabolites, rigorous assignment of the ^{13}C NMR spectrum was required as a first step. It was expected that comparison of the signals in LL-D253α and its diacetate would aid this assignment. Large changes in the ^{13}C chemical shift values of systems such as **1** are expected when the chelation of the *peri*-hydroxy function is removed: *e.g.* when 2-hydroxyacetophenone is acetylated the carbonyl, C-1 and C-2 resonances at 204, 119 and 160 ppm respectively move to 197, 130 and 147 ppm respectively.[5] However, no such changes were observed in the ^{13}C NMR spectra of LL-D253α and its diacetate derivative. This prompted a re-examination of the structures of LL-D253α and we now report full details of ^{13}C NMR studies on LL-D253α which necessitate revision of the structure to **6** and synthetic work which gives *inter alia* unambiguous syntheses of structures **1**, **4** and **6**.[6]

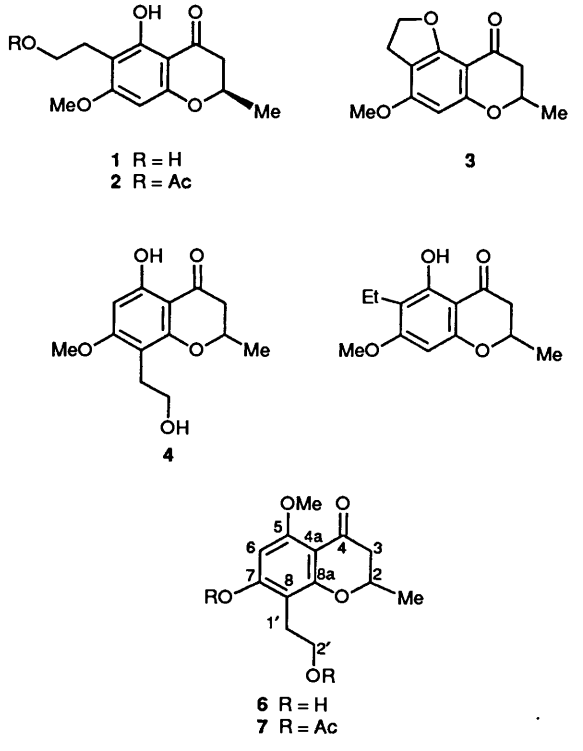

Fig. 1 shows the high frequency region of the fully ^{1}H coupled ^{13}C NMR spectrum of LL-D253α diacetate **7** and the results of a series of specific low-power decoupling experiments. This technique has proved particularly valuable in both structural[7] and spectral[8] assignment studies in our experience. All the aromatic carbons give characteristic multiplet patterns due to long-range coupling apart from C-6 which appears as a doublet [$^1J(^{13}C–^1H)$ 126 Hz] due to one bond ^{13}C–^{1}H coupling. Irradiation of the methine proton (2-H) caused a marked sharpening of the diffuse triplet at 161.5 ppm which must, therefore, be due to C-8a. However, irradiation of the benzylic methylene hydrogen (1′-CH_2) collapsed the same signal to a broad singlet. The hydroxyethyl side-chain must, therefore, be placed at C-8. This irradiation also affected two other signals: that at 154.5 ppm which changes from a quartet to a doublet, and that at 110.2 ppm (multiplet to quartet). These can be assigned to C-7 and C-8 on chemical-shift grounds. However, C-7 does not carry the methoxy group as decoupling of the methoxy protons affects only the signal at 159.3 ppm (quintet to doublet) which must be assigned to C-5 by elimination of the other two oxygenated aromatic carbons. Decoupling of the aromatic proton gives results entirely consistent with its revised

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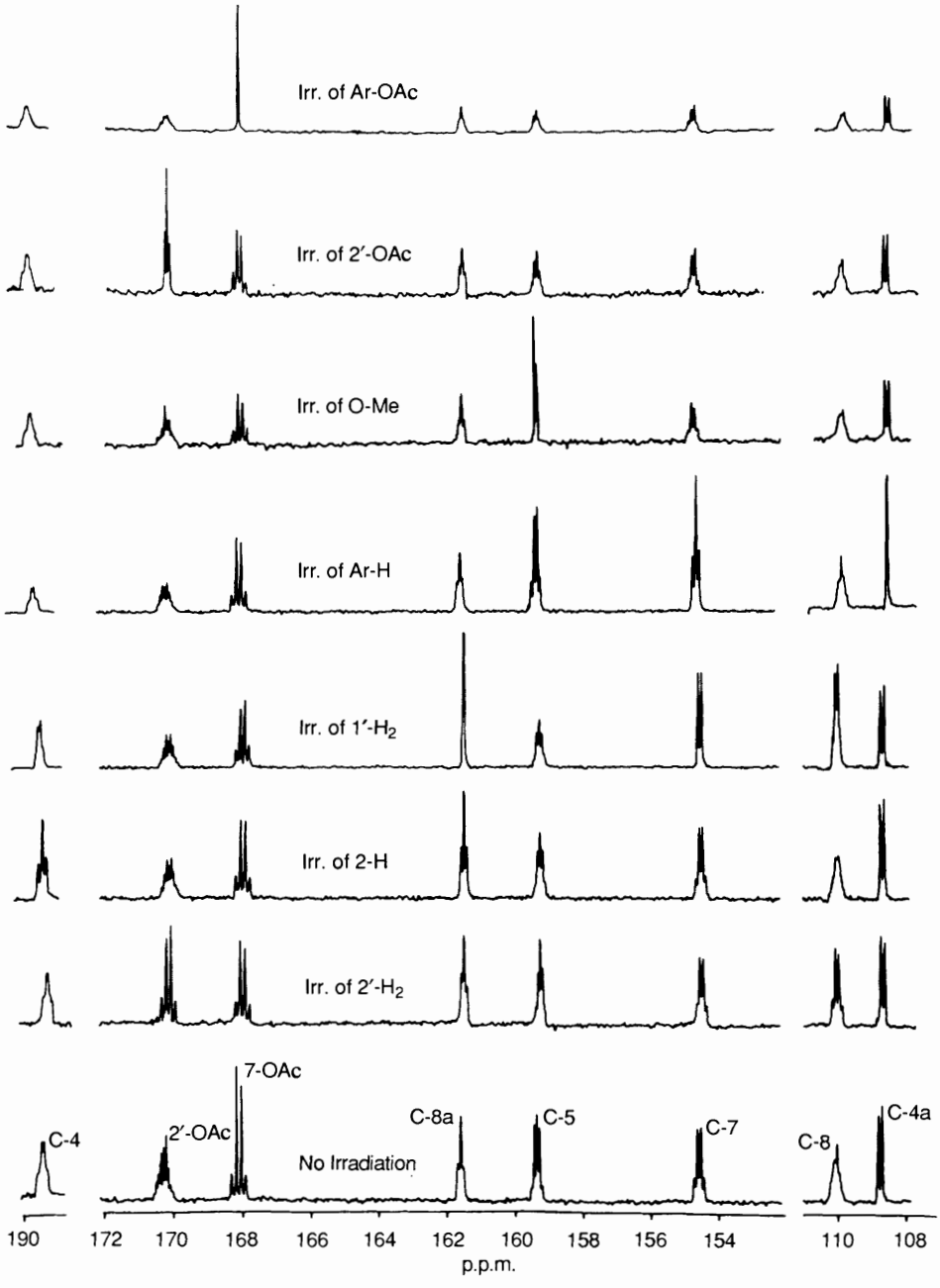


Fig. 1 The lowfield region of the fully ^1H coupled 50 MHz, ^{13}C NMR spectrum of LL-D253α diacetate **7** and the results of selective low power ^1H-decoupling experiments

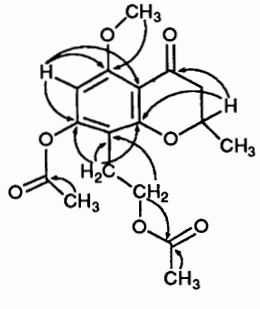
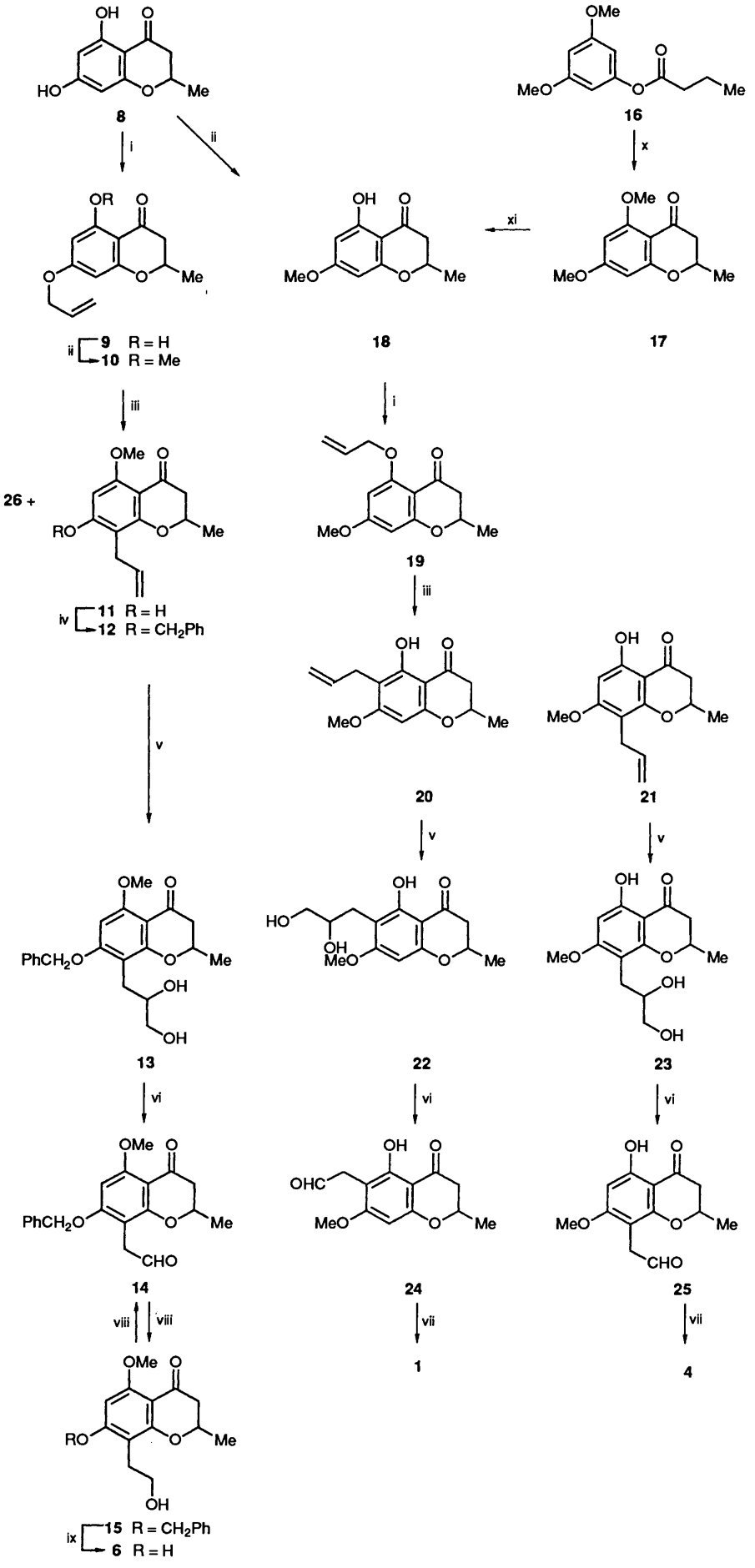


Fig. 2 Long-range ^1H–^{13}C couplings in LL-D253α diacetate **7** identified by selective ^1H-decoupling experiments

position at C-6. Three signals are affected: at 159.3 ppm (quintet to quartet, C–S); at 154.5 ppm (quartet to triplet, C-7); and at 108.8 ppm (doublet to singlet, C-4a); C-8 and C-8a were unaffected. Decoupling of the side-chain methylene (2′-CH_2) sharpens the signal at 110.2 ppm (multiplet to quartet, C-8) and also allows the assignment of the aliphatic acetate carbonyl to the signal at 170.2 ppm (multiplet to quartet). Finally, irradiation of 2-H also caused the carbonyl resonance at 189.4 ppm to sharpen to a triplet, the remaining coupling being the two-bond coupling to the C-3 methylene hydrogens. All the carbon–hydrogen couplings established by these experiments are summarised in Fig. 2. These couplings are entirely consistent with the revised structure **7** for LL-D253α diacetate and hence **6** for LL-D253α itself. It is noteworthy that several two-bond couplings to aromatic hydrogens are observable in contrast to the usually observed three-bond couplings; this has been previously noted in phenolic acetates.[9]

In order to confirm this structural reassignment we have synthesised both the revised structure and the originally assigned structure **1** by unambiguous routes (Scheme 1). In the



Scheme 1 *Reagents and conditions:* i, $H_2C = CHCH_2Br$, K_2CO_3; ii, MeI, K_2CO_3; iii, heat; iv, $PhCH_2Br$, K_2CO_3; v, OsO_4; vi, $NaIO_4$; $NaBH_4$, THF; viii, pyridinium chlorochromate; ix, H_2, Pd (C); x, *hv*, C_6H_6, NaOH; xi, BCl_3, CH_2Cl_2

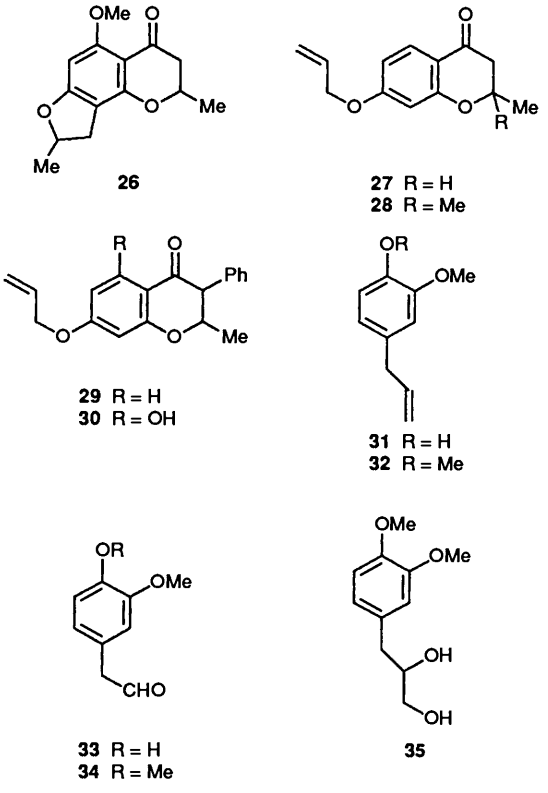
course of this work, the alternative structure **4** and the methyl ether **50** of the ethyl analogue of **1** have also been synthesised.

For the synthesis of **1** and **6**, the initial objective was 5,7-dihydroxy-2-methylchroman-4-one **8**. The wide range of synthetic approaches towards chroman-4-ones has been reviewed.[10–12] *O*-Alkylation of such compounds is known to take place preferentially at the 7-position so selective mono-methylation or mono-allylation is possible.[13] Further allylation or methylation would produce the isomeric structures **10** and **19**. Claisen rearrangement and oxidative cleavage of the resultant *C*-alkyl group would allow elaboration of the hydroxyethyl side-chain.[14] The starting chromanone was prepared by modification of a published procedure[15] from phloroglucinol and crotonic anhydride in a disappointing yield of 36% after a difficult work-up. Boron trifluoride has been used as catalyst in the synthesis of 5,7-dihydroxy-2,2-dimethylchroman-4-one from phloroglucinol and 3,3-dimethylacrylic acid.[16] This procedure was repeated for crotonic acid and phloroglucinol; the result was a similar yield of **8** and the same problems with product isolation. Finally, the reaction of phloroglucinol with crotonic acid, methanesulfonic acid and phosphorus pentoxide was investigated.[17] This gave a much improved yield and an easier isolation of product. All attempts to produce **8** by reduction of the readily available 5,7-dihydroxy-2-methylchromone by catalytic hydrogenation[18] or by other methods known to be effective for the reduction of similar double bonds[19] failed in our hands.

Reaction of the dihydroxychromanone **8** with 1 equiv. of allyl bromide gave the monoallyl ether **9** which on treatment with methyl iodide gave **10** in 81% yield. This compound could be prepared by successive treatment with allyl bromide and methyl iodide in a one-pot reaction. However, the overall yield was not improved. Claisen rearrangement of the allyl ether **10** gave only the 8-allyl compound **11**. Previous work on the Claisen rearrangement of 7-allyloxychromanones resulted in the formation of the 8-allyl-7-hydroxychromones unless the 8-position was already substituted.[20] The 7-allyloxychromanones, **27** and **28** and the 7-allyloxyisoflavanones **29** and **30** all gave their 8-allyl products when heated.[21] In view of this consistent background, the *C*-allyl compound obtained in 68% yield from pyrolysis of **10** was designated structure **11**. The pyrolysis also produced minor quantities of a second product which on the basis of its ^{1}H NMR spectrum was assigned the dihydrofuran structure **26**. It is presumably obtained from the initial product **11** by intramolecular addition to the allyl double bond.

Attempts to cleave the double bond in **11** to produce the aldehyde by ozonolysis followed by reductive work-up using dimethyl sulfide gave only an intractable mixture. A series of experiments were carried out using eugenol **31** as a model to optimise conditions for the cleavage of the double bond. Ozonolysis of either eugenol on the corresponding methyl ether **32** gave no definable products. The aldehyde **33** has been prepared but is known to be unstable.[22] Using a catalytic amount of osmium tetroxide in an excess of periodate, a procedure successfully applied to a similar allyl compound,[23] gave mostly starting material when eugenol was the substrate. Finally, the aldehyde **34** was obtained in quantitative yield by the addition of 1 equiv. of osmium tetroxide to eugenol methyl ether followed by periodate cleavage of the intermediate diol **35**.

In the light of these results it was decided to protect the phenolic hydroxy of the 8-allylchromanone **11** before oxidative cleavage of the allyl group. Reaction with benzyl bromide gave the benzyl ether **12** which was treated with 1 equiv. of osmium tetroxide to give the diol **13** as a mixture of diastereoisomers. The diol **13** was cleaved with sodium periodate[24] to give a quantitative yield of the aldehyde **14** which was identified by its IR carbonyl band at 1724 cm^{-1}, by the lowfield triplet (9.60 ppm) in its ^{1}H NMR spectrum and by the ^{13}C NMR signal at 199.4 ppm. The same compound was obtained by pyridinium chlorochromate (PCC) oxidation[25] of the benzyl ether **15** of LL-D253α. Attempts to recrystallise the aldehyde resulted in decomposition. The aldehyde carbonyl was selectively reduced using sodium borohydride in tetrahydrofuran[26] to give the hydroxyethyl compound **15** in 72% yield. Hydrogenolysis of **15** gave racemic LL-D253α **6** in 63% yield.



26

27 R = H
28 R = Me

29 R = H
30 R = OH

31 R = H
32 R = Me

33 R = H
34 R = Me

35

Synthesis of the original proposed structure **1** was next investigated. 5-Allyloxy-7-methoxy-2-methylchroman-4-one **19** was prepared in 62% yield by a one-pot reaction of **8**, first with 1 equiv. of methyl iodide and then with an excess of allyl bromide. Although the intermediate methyl ether **18** was not isolated, it was subsequently prepared *via* photo-Fries rearrangement of the aryl acrylate **16**[27] in a two-phase (benzene–aqueous hydroxide) system. This procedure was reported[28] to give high yields of chroman-4-ones. The main advantage of this preparation was the ease of isolation of the product, the known 5,7-dimethoxy-2-methylchroman-4-one **17**. Unfortunately, the best yields obtained in our hands was only 21%. However, treatment of the dimethyl ether with boron trichloride[29] gave the 5-hydroxy compound **18** in 96% yield. The ^{1}H NMR showed a sharp lowfield signal (12.13 ppm) characteristic of such chelated phenols.

Claisen rearrangement of the 5-allyloxy ether **19** on a small scale gave a quantitative yield of a single compound, subsequently identified as the desired 6-allyl compound **20**. However, repetition of the reaction on a larger scale gave two products which were separated, with some difficulty, by repeated TLC. The major product (46%) proved to be the same as that obtained in the small-scale experiment. It was accompanied by a minor (25%) component which had very similar spectroscopic properties and was assigned the 8-allyl structure **21**. These assignments were subsequently confirmed on conversion of both **20** and **21** into the corresponding hydroxyethyl derivatives *via* osmium tetroxide oxidation to the vicinal diols, **22** and **23**; periodate cleavage to the aldehydes, **24** and **25**; and borohydride reduction to the alcohols, **1** and **4**.

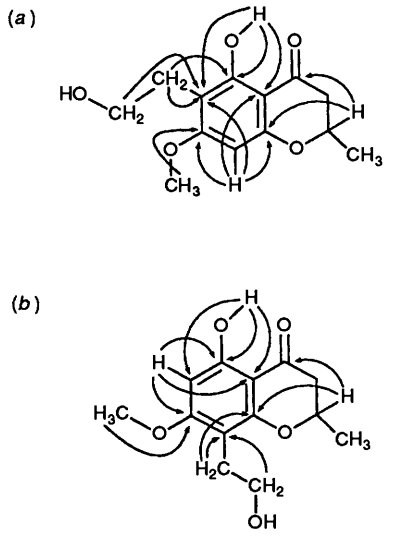
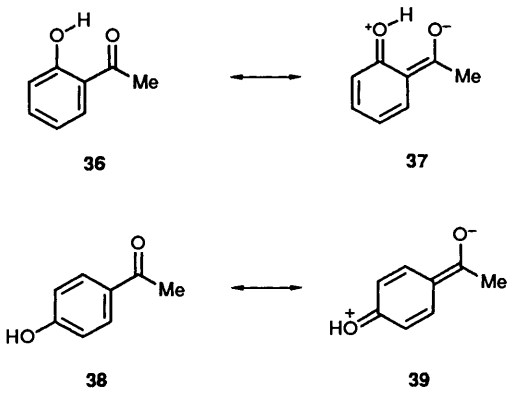


Fig. 3 Long-range couplings observed in the fully ^{1}H-coupled ^{13}C NMR spectra of (a) 5-hydroxy-6-(2-hydroxyethyl)-7-methoxy-2-methylchroman-4-one **1**, and (b) 5-hydroxy-8-(2-hydroxyethyl)-7-methoxy-2-methylchroman-4-one **4**



Prior protection of the phenolic hydroxy groups proved unnecessary in these compounds.

Structures **1** and **4** were confirmed by examination of the fully ^{1}H-coupled ^{13}C NMR spectra by addition of D_2O and selective low-power proton-decoupling experiments. In contrast to LL-D253α both compounds are readily soluble in chloroform. On addition of D_2O to a deuteriochloroform solution of **1**, the product from the major isomer **20** in the Claisen rearrangement of **19**, three signals were noticeably modified including the two due to the non-protonated, non-oxygenated aromatic carbons at 102.7 and 106.6 ppm which sharpen, respectively, to a double from a triplet, and a quartet from a multiplet. The only other signal affected is that at 160.8 ppm which simplifies from a quartet to a triplet and also displays a significant (0.2 ppm) upfield shift. This allows assignment of the signal to C-5. The presence of the hydroxyethyl side-chain at C-6 is confirmed by the removal of the remaining triplet coupling on C-5 by irradiation of the benzylic methylene hydrogens. On decoupling 2-H the only aromatic signal to be affected is the doublet at 161.9 ppm which markedly sharpens and so must be assigned to C-8a. The doublet coupling is removed on irradiation of the aromatic proton and removal of the expected three-bond coupling. These observations effectively determine structure **1** for this compound. The couplings revealed by these and other decoupling experiments are summarised in Fig. 3a.

A similar series of experiments was carried out on the hydroxyethyl compound **4** obtained from the minor product of the Claisen rearrangement of **19**. The results are summarised in Fig. 3b. The protonated aromatic carbon displays a long-range coupling, lost on addition of D_2O, to the phenolic proton. In addition the only aromatic carbon (at 159.5 ppm) affected by the decoupling of 2-H is also affected by the decoupling of the benzylic hydrogens.

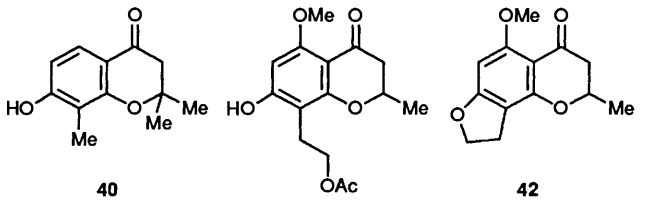
Compounds **1** and **4**, therefore, correspond to the structures previously proposed for LL-D253α. They clearly differ from the natural product in their solubility in chloroform and the presence of chelated hydroxy protons in the ^{1}H NMR spectrum at 12.13 and 12.12 ppm, respectively. The ^{1}H NMR spectrum of LL-D253α has previously been obtained in deuteriomethanol. Its spectrum was obtained in deuteriochloroform by prolonged accumulation at 300 MHz. No downfield chelated hydroxy was present, instead an exchangeable signal was evident at 3.48 ppm. The other notable feature of this spectrum was the appearance of the signals arising from the two methylene groups of the hydroxyethyl side-chain. These each gave 16-line multiplets due to an ABXY spin-system which suggests that bond rotation of the hydroxyethyl side-chain is restricted, probably by intramolecular hydrogen bonding. The ^{1}H NMR spectrum of the diacetate **7** shows simple triplets for the side-chain methylene hydrogens.

The evidence which led to the previous assignment of the *ortho*-hydroxy carbonyl structure **1** for LL-D253α must be considered, particularly the IR data. Carbonyl absorptions around 1640 cm^{-1} are frequently invoked as evidence for chelation indicative of *ortho*-hydroxy carbonyl structures, especially if the frequency rises on either methylation or acetylation.[30–32] However, it appears that the low frequency of such a carbonyl, *e.g.* that in 2-hydroxyacetophenone **36**, is *not* due to hydrogen bonding, but to the contribution of the resonance form **37** which reduces the double-bond character of the carbonyl group.[33–34] A similar resonance form **39** can be drawn for 4-hydroxyacetophenone **38**. Examination of published IR data for various acetophenones[35] provides support for this suggestion. The substitution of acetophenone with a hydroxy at either the *ortho* or *para* ring positions produces similar low frequency shifts (*ca.* 50 cm^{-1}). *meta*-Substitution produces a much smaller shift. Multiple substitution in the *ortho* and *para* positions has only a small effect, *i.e.* the shifts are not additive. In contrast, the carbonyl absorptions of the *ortho*, *meta* and *para* methyl ethers are all around 1675 cm^{-1}. A rather closer example[36] of the effect of *para*-hydroxy substitution is found in 7-hydroxy-2,2,8-trimethylchroman-4-one **40** where the pyranone carbonyl occurs at 1645 cm^{-1}. Therefore the IR data for LL-D253α, and its diacetate and methyl ether are consistent with the revised structure **6**. In the light of these results the structures of the co-metabolites of LL-D253α: LL-D253β, LL-D253γ and the corresponding ethyl analogue should be revised to **41**, **42** and **43** respectively.

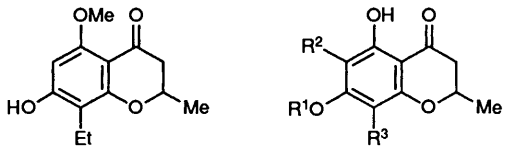
The other evidence used in placing the substituents on the chromanone ring was the Gibbs test.[2] Erroneous positive indications have been previously reported and[37,38] it has been suggested that the test is best carried out in conjunction with a UV spectrometer to increase its reliability.[39]

In the course of attempts to prepare 8-substituted chromanones as potential intermediates for biosynthetic studies,[40] a number of other chromanone derivatives were obtained. The 8-acetyl chromanone **45** is a likely biosynthetic intermediate. Friedel–Crafts acylation of 5,7-dihydroxy-2-methylchroman-4-one gave two products, **45** and **46** in equimolar amounts. Their structures were assigned on the basis of the long-range couplings observed in the fully ^{1}H coupled ^{13}C NMR spectrum.

In view of the lack of selectivity obtained in the acylation, it was hoped that Fries rearrangement of 7-acetoxy-5-hydroxy-2-methylchroman-4-one **44** would give the desired 8-acetyl isomer **45** exclusively. Acetylation of **8** gave the desired 7-acetoxy derivative **44** as expected. However, attempted Fries rearrange-



40 41 42

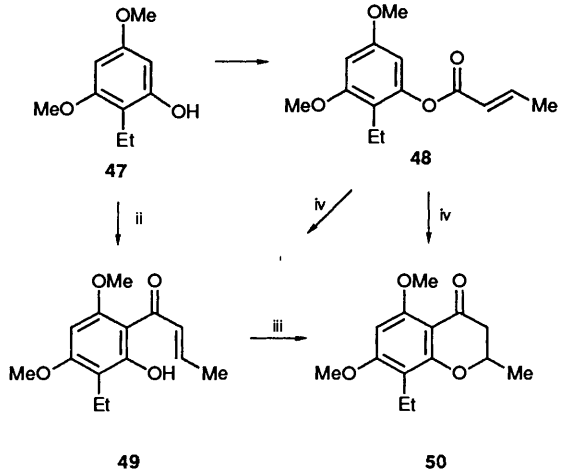


43

44 R^1 = Ac, R^2 = R^3 = H
45 R^1 = R^2 = H, R^3 = Ac
46 R^1 = R^3 = H, R^2 = Ac

ment using aluminium chloride catalyst gave the deacylated compound **8** as the only identifiable product. Attempted rearrangement using the photo-Fries conditions[41] gave no reaction. These results are consistent with a report that an *ortho* or *para* carbonyl functionality are known to hinder or prevent the Fries rearrangement.[42]

Support for this explanation was obtained from work on the synthesis of the *C*-ethyl compound **50**, the methyl ether of **43** which has been reported as a co-metabolite of LL-D253α and LL-D253γ in *Phoma violacea*. This was obtained, in low yield, by Fries rearrangement of the crotonate ester **48** of 2-hydroxy-4,6-dimethoxyethylbenzene **47** (Scheme 2). Compound **50** was also prepared in higher yield *via* the 'magnesium directed' Friedel–Crafts acylation of **47**.[43] The crotonylphenol **49** was obtained, along with a small amount of the chromanone **50**. The former exhibited similar spectral properties to those of its desethyl analogue, a metabolite of the herbs *Dysophilla stellata*[44] and *Dysophilla tometosa*.[45] The crotonylphenol **49** was completely converted into the desired chromanone **50** on stirring in dilute aqueous sodium hydroxide.



47 48 49 50

Scheme 2 *Reagents and conditions:* i, MeCH = CHCOCl, Mg, toluene; ii, MgBr, MeCH = CHCOCl; iii, NaOMe, MeOH; iv, heat

Experimental

M.p.s were determined on a Reichert hot-stage microscope and are uncorrected. Microanalyses were performed on a Perkin-Elmer 204 analyser. A Varian DMS 90 spectrophotometer was used to obtain UV/visible spectra; baseline correction for solvent absorption was carried out; ε is in units of dm^3 mol^{-1} cm^{-1} (log ε quoted below). IR spectra were taken on a Perkin-Elmer 781 spectrophotometer and referenced against the polystyrene absorption at 1601 cm^{-1}. ^1H NMR spectra were obtained from various instruments: Varian EM 360 and HA 100 continuous-wave machines and Bruker WP 80 SY, WP 200 SY, WM/WB 300 and WH 360 Fourier-transform machines. Carbon-13 NMR spectra were obtained from: Varian XL 100 and CFT 20 and Bruker WP 200 SY, WH 360 and WH 400 Fourier-transform machines. ^2H NMR spectra were obtained on a Bruker WH 360, operating in this case without a frequency lock. In all cases, quoted chemical shifts are relative to tetramethylsilane, δ_H and δ_C = 0.0; *J*-values are recorded in Hz. Mass spectra and exact mass determinations were taken on a A.E.I. MS 902 high-resolution instrument, ionising by electron impact. Peak intensities are expressed as percentages relative to the base peak at 100%.

Unless otherwise specified, TLC was performed using either analytical (5 × 20 cm) or preparative (20 × 20 cm) glass plates coated with a 0.5-mm layer of silica gel (Merck Art. 7730 Kieselgel 60 GF_{254} or Fluka AG 60765 Kieselgel GF 254). Where precoated metal strips are specified, Merck Art. 5548 HP-TLC-Alufolien Kieselgel 60 F 254 was used. Unless stated otherwise, UV light of wavelength 254 nm was used to visualise chromatograms.

Production and Isolation of LL-D253α.—Phoma pigmentivora (QM 502) was stored at 4 °C under liquid paraffin on slopes of corn-meal agar (Oxoid CM 103). A spore suspension in distilled water was used as the inoculum for a seed culture grown in 250 cm^3 Erlenmeyer flasks on an orbital shaker. Each flask contained 75 cm^3 of the medium–ammonium tartrate 0.2% (w/v), magnesium sulfate (heptahydrate) 0.05% (w/v), potassium chloride 0.05% (w/v), potassium orthophosphate 0.1% (w/v), ferrous sulfate (heptahydrate) 0.001% (w/v), glucose 5.0% (w/v), corn steep liquor 1.0% (w/v), and distilled water to 100%. (The pH was adjusted to 6.5 with 2 mol dm^{-3} aqueous sodium hydroxide.)

After 3–4 days incubation at 20 °C in constant light, the suspension of mycelium was used to inoculate further such flasks of the same medium which were, in turn, incubated under the same conditions for up to 12 days. The usual growth period was 5 days by which time the medium had turned appreciably darker in appearance.

The mycelium was filtered off (Whatman's No. 1) and washed with a little water. The medium and washings were acidified to pH *ca.* 2 with dilute (2 mol dm^{-3}) hydrochloride acid and extracted with ethyl acetate (3 or 4 times with one-third of the liquor volume). After the extract had been dried ($MgSO_4$), the solvent was removed under reduced pressure to leave a brown gum, the constituents of which were separated by preparative TLC, methanol–chloroform (10:90) being used as developer. The band at R_F *ca.* 0.5 was eluted with methanol–ethyl acetate (5:95) to give, on evaporation of the solvent, LL-D253α as a white crystalline solid. Yields were variable but were usually between 200 and 400 mg dm^{-3}. [Further purification by TLC (if required) was effected using acetone–chloroform (20:80) with which two developments were necessary to give R_F = 0.5.] Recrystallisation from ethyl acetate–methanol afforded white needles, m.p. 192.5–193 °C (lit.,[1] 188–188.5 °C; lit.,[3] 191–193 °C). Spectral data were identical with those of an authentic sample (Found: C, 61.7; H, 6.6. Calc. for $C_{13}H_{16}O_5$; 61.9; H, 6.39%); λ_{max}(MeOH)/nm 316, 285, 230 and 213; ν_{max}(KBr)/cm^{-1} 3160br m, 1652m, 1595s, 1290m and 1116m; δ_H(300 MHz; $CDCl_3$) 1.44 (3 H, d, *J* 6.3, $CHCH_3$), 2.49–2.63 (2 H, AB of ABX, CH_2), 2.79–3.00 (2 H, m, 16 lines, $ArCH_2$), 3.48 (s, OH), 3.84 (3 H, s, OCH_3), 3.84–4.00 (2 H, m, CH_2OH), 4.38–4.52 (1 H, m, 2-H) and 6.13 (1 H, s, ArH); δ_C[20 MHz; $(CD_3)_2SO$]

20.5 (q), 26.5 (t), 45.2 (t), 55.4 (q), 60.1 (t), 73.3 (d), 92.7 (d), 104.5 (s), 104.7 (s), 159.9 (s), 162.0 (s), 162.2 (s) and 188.5 (s); *m/z* (%) 252 (53), 221 (83) and 179 (100).

LL-D253α Diacetate **7**.—LL-D253α **6** (250 mg, 0.99 mmol) was dissolved in redistilled acetic anhydride (5 cm^3); pyridine (5 drops) was added, and the mixture was heated under gentle reflux for 10 min with careful exclusion of moisture. The solvents were removed under reduced pressure, the final traces being azeotroped with chloroform and carbon tetrachloride, to leave LL-D253α diacetate **7** (336 mg, 1.00 mmol, 100%), as a white crystalline solid, m.p. 120.5–122.5 °C. Recrystallisation from ethyl acetate–hexane yielded small white prisms, m.p. 122.5–124.5 °C (lit.,[1] 121–122 °C). (If the starting material was not completely pure, the diacetate could be purified by preparative TLC, with methanol–chloroform (2:98) as developer, R_f 0.7, and eluting with ethyl acetate); ν_{max}(KBr)/cm^{-1} 1767s, 1734s, 1689s and 1591s; δ_H(360 MHz; $CDCl_3$) 1.48 (3 H, d, *J* 6.3, $CHCH_3$), 2.01 (3 H, s, CH_2OCOCH_3), 2.34 (3 H, s, $ArOCOCH_3$), 2.57–2.67 (2 H, AB of ABX, 3-CH_2), 2.82 (2 H, t, *J* 7.0, $ArCH_2$), 3.85 (3 H, s, OCH_3), 4.14 (2 H, t, *J* 7.0, CH_2OAc), 4.50–4.61 (1 H, m, 2-H) and 6.26 (1 H, s, ArH); δ_C(50 MHz; $CDCl_3$) 20.0 (q), 20.2 (q), 22.7 (t), 44.9 (t), 55.5 (q), 62.2 (t), 73.6 (d), 98.5 (d), 108.8 (s), 110.2 (s), 154.5 (s), 159.3 (s), 161.5 (s), 168.0 (s), 170.2 (s) and 189.4 (s).

Crotonic Anhydride.—Crotonic acid (40 g, 0.47 mol) and acetic anhydride (148 g, 1.45 mol) were heated together under reflux for 47 h. Precautions were taken to exclude moisture. The bulk of the acetic anhydride was then removed by distillation; the concentrate was taken up in dry ether (200 cm^3) and shaken with anhydrous sodium carbonate. After filtration, the ether was removed under reduced pressure and the residue was distilled under reduced pressure through a short Vigreux column. The fraction boiling in the range 128–157 °C at 54 mmHg was retained. NMR spectroscopy confirmed that the product was practically pure crotonic anhydride (20.1 g, 0.131 mol, 56%) (lit.,[46] b.p. 128–130 °C at 19 mmHg); δ_H(60 MHz; $CDCl_3$) 1.83 (3 H, dd, *J* 7, 1.5, $CHCH_3$), 5.87 (1 H, dq, *J* 16, 1.5, COCH) and 7.11 (1 H, dq, *J* 16, 7, $CHCH_3$).

5,7-Dihydroxy-2-methylchroman-4-one **8**.—(*a*) Anhydrous phloroglucinol **2** (7.67 g, 61 mmol) and anhydrous aluminium trichloride (25 g, 187 mmol) were stirred in dry redistilled nitrobenzene (75 cm^3) at room temperature until dissolved, to give a dark-green solution. Moisture was carefully excluded. Crotonic anhydride (9.44 g, 61 mmol) and a solution of anhydrous aluminium trichloride (16.4 g, 123 mmol) in nitrobenzene (60 cm^3) were then added simultaneously from separate dropping funnels (with stirring) over 1 h. When the additions were complete the mixture was heated to 50 °C and stirred at this temperature for 18 h after which time analytical TLC, with acetone–chloroform (20:80) as developer, indicated that no phloroglucinol remained (R_f 0.15). A major product at R_f 0.32 was indicated.

After cooling, the mixture was decanted into a bath of ice (250 cm^3)–dilute hydrochloric acid (4 mol dm^{-3}; 250 cm^3). The nitrobenzene layer was separated and washed with dilute HCl (4 mol dm^{-3}; 100 cm^3) and the combined aqueous layers were then extracted with ethyl acetate (3 × 100 cm^3). The extract was concentrated under reduced pressure to *ca.* 200 cm^3 and washed with dilute HCl (1 mol dm^{-3}; 4 × 100 cm^3) to remove any remaining aluminium trichloride. The nitrobenzene was removed from the combined organic layers by prolonged steam-distillation to leave a residue of *ca.* 120 cm^3. This was decanted, while still hot, from a brown oil and refrigerated overnight to yield brown crystals (1.20 g). These were purified by sublimation (170 °C at 0.2 mmHg) to give an off-white crystalline sublimate (1.06 g). Analytical TLC of the brown oil indicated that its major component was the same as the crystalline material. The oil was, therefore, purified by sublimation under the same conditions to afford further crystalline product (3.17 g): 5,7-dihydroxy-2-methylchroman-4-one **8** (total yield 4.23 g, 22 mmol, 36%). Recrystallisation from aqueous ethanol gave white needles, m.p. 176–178 °C (lit.,[29] 176–177 °C); ν(KBr)/cm^{-1} 3160vbr m, 1633s, 1605s, and 1166s; δ_{CH}[60 MHz, $CDCl_3$–[$^2H_6$]-DMSO (70:30)] 1.47 (3 H, d, *J* 6, $CHCH_3$), 2.62 (2 H, AB of ABX, 3-CH_2) 4.2–4.9 (1 H, m, 2-H), 5.98 (2 H, s, 2 × ArH), 10.36 (1 H, br s, ex, 7-OH) and 12.21 (1 H, s, ex, 5-OH).

(*b*) To dry phloroglucinol (2.662 g, 21.13 mmol) and dry crotonic acid (1.909 g, 22.20 mmol) in a three-necked flask was added dry nitrobenzene (100 cm^3). The mixture was stirred for 1 h and then cooled to 0 °C. To the yellow suspension was added boron trifluoride–diethyl ether (12 cm^3) over 20 min. The resulting brown solution was heated at 110 °C for 2.5 h to give a green solution. This was poured into saturated aqueous sodium acetate (200 cm^3).

Aqueous sodium hydroxide (2 mol dm^{-3}; 100 cm^3) was added, and this was extracted into ether (4 × 500 cm^3 portions). The alkaline solution was acidified (2 mol dm^{-3} hydrochloric acid) and thrice extracted into ethyl acetate. The combined organic extracts were dried and concentrated under reduced pressure to give a brown gum. This was purified as described above to give a white solid (1.31 g, 32%) with the same NMR and TLC characteristics as the material obtained in part (*a*) above.

(*c*) Methanesulfonic acid (80 cm^3) and phosphorus pentoxide (4.0 g) were heated to 70 °C under a flow of dry nitrogen. Anhydrous phloroglucinol (6.18 g, 49.0 mmol) and dry crotonic acid (4.225 g, 49.1 mmol) were mixed and added. After being heated at 70 °C for 45 min this was allowed to cool, and the red solution was poured onto ice–water (600 cm^3), to give an orange precipitate. This was extracted into ether (3 × 250 cm^3 portions) which were washed with water (2 × 150 cm^3 portions) and brine (150 cm^3). The ethereal solution was dried and concentrated to yield a red oil (8.757 g). This was purified by flash chromatography, using as eluent light petroleum (40–60 °C) with an increasing proportion of ether. White crystals were obtained (5.76 g, 60%) of material with the same NMR and TLC characteristics as that described in (*a*) and (*b*) above for the chroman-4-one **8**.

7-Allyloxy-5-hydroxy-2-methylchroman-4-one **9**.—The chroman-4-one **8** (1.01 g, 5.21 mmol), allyl bromide (0.50 cm^3, 0.71 g, 5.87 mmol) and anhydrous K_2CO_3 (3.00 g) were stirred and heated in dry acetone (75 cm^3) under reflux, moisture being excluded. The progress of the reaction was followed by analytical TLC with methanol–chloroform (10:90) as developer (starting material, R_f 0.45; major product, R_f 0.71). After 17.5 h the flask was allowed to cool and the inorganic salts were filtered off and washed with further acetone. The combined filtrate and washings were concentrated under reduced pressure to give a brown oil which, on the addition of ice, formed pale brown crystals of the title compound **9** (0.77 g, 3.31 mmol, 64%). Sublimation (60 °C at 0.1 mmHg) gave white needles, m.p. 55–58 °C) (Found: M^+, 234.0861. $C_{13}H_{14}O_4$ requires *M*, 234.0892); λ_{max}(MeOH)/nm (log ε) 317sh (3.52), 286 (4.28), 266sh (4.21) and 215 (4.35); ν_{max}(KBr)/cm^{-1} 1644 (s), 1609m sh, 1575m, 1306m and 1164s; δ_H(60 MHz; $CDCl_3$) 1.52 (3 H, d, *J* 6, $CHCH_3$), 2.67 (2 H, AB of ABX, 3-CH_2), 4.58 (2 H, dm, *J* 5, OCH_2), 4.35–4.9 (1 H, m, 2-CH), 5.2–5.65 (2 H, m, $CH{=}CH_2$), 5.7–6.4 (1 H, m, $CH{=}CH_2$), 6.10 (2 H, AB, *J* 2, 2 × ArH) and 12.04 (s, 5-OH); *m/z* (%) 234 (M^+, 100), 219 (22), 194 (14), 192 (28), 164 (16), 123 (17), 82 (17), 69 (25) and 41 (53).

7-Allyloxy-5-methoxy-2-methylchroman-4-one **10**.—The

chroman-4-one **9** (582 mg, 2.49 mmol), methyl iodide (0.50 cm^3, 1.14 g, 8.03 mmol) and anhydrous K_2CO_3 (2.06 g) were stirred and heated together in dry acetone (75 cm^3) under reflux, moisture being excluded. The progress of the reaction was monitored by analytical TLC, with acetone–ethyl acetate–light petroleum (b.p. 30–40 °C) (5:45:50) as developer. The product was slightly more polar than the phenol. After 24 h the flask was cooled and the inorganic salts were filtered off and washed with further acetone. The combined filtrate and washings were concentrated under reduced pressure and the residue taken up in diethyl ether (100 cm^3) and washed with water (3 × 20 cm^3). After the solution had been dried ($MgSO_4$) the ether was removed to give a yellow oil (1.02 g). Preparative TLC with ethyl acetate–diethyl ether (20:80) as developer yielded the *title compound* **10** (498 mg, 2.01 mmol, 81%) (R_f 0.8) as a yellow oil which crystallised on treatment with light petroleum (b.p. 40–60 °C). An analytical sample, crystallising as white prisms from diethyl ether–hexane, had m.p. 83.5–84.5 °C (Found: C, 67.7; H, 6.65. $C_{14}H_{16}O_4$ requires C, 67.73; H, 6.50%); λ_{max}(MeOH)/nm (log ε) 310sh (3.62), 281 (4.25), 225 (4.25) and 213 (4.32); ν_{max}(KBr)/cm^{-1} 1666s, 1610s and 1574s; δ_H(100 MHz; $CDCl_3$) 1.43 (3 H, d, *J* 6, C–CH_3), 2.57 (2 H, AB of ABX, 3-CH_2), 3.38 (3 H, s, OCH_3), 4.3–4.7 (1 H, m, 2-H), 4.50 (2 H, dt, *J* 5, 1.5, OCH_2), 5.29 (1 H, dm, *J* 10, CH=C*H cis*), 5.38 (1 H, dm, *J* 18, CH=C*H trans*), 5.8–6.2 (1 H, m, CH_2=CH_2) and 6.04 (2 H, s, 2 × ArH); δ_C(20 MHz; $CDCl_3$ 20.4 (q), 45.3 (t), 55.7 (q), 68.6 (t), 73.5 (d), 92.9 (d), 93.7 (d), 105.5 (s), 118.0 (t), 131.9 (d), 161.8 (s), 164.3 (s), 164.7 (s) and 189.3 (s); *m/z* (%) 248 (M^+, 100), 206 (29), 179 (17), 137 (20), 69 (29) and 41 (56).

8-Allyl-5-hydroxy-5-methoxy-2-methylchroman-4-one **11**.—The chroman-4-one **10** (425 mg, 1.71 mmol), sealed *in vacuo* (0.5 mmMg) in a strong glass tube (8 mm i.d. × 10 cm) was heated (200 °C) for 50 min to produce a red liquid which solidified on cooling. Flash chromatography eluting with 10% acetone in chloroform yielded the *title compound* **11** as a clear gum which crystallized with time (287 mg, 1.16 mmol, 68%). This compound could also be purified by preparative TLC with acetone–chloroform (20:80) as developer (R_f 0.31 *cf.* starting allyl ether at R_f 0.54). Sublimation (180 °C at 0.02 mmHg, 84%) gave fine white needles, m.p. 198–199.5 °C (decomp.) (Found: C, 67.9; H, 6.6; $C_{14}H_{16}O_4$ requires C, 67.73; H, 6.50%); λ_{max}(MeOH)/nm (log ε), 315sh (3.65), 286 (4.19), 232sh (4.12) and 214 (4.25); ν_{max}(KBr)/cm^{-1} 3200m br, 1646s, 1593s, 1280m and 1122m; δ_H[80 MHz; $(CD_3)_2CO$] 1.43 (3 H, d, *J* 6.2, C–CH_3), 2.47 (2 H, AB of ABX, 3-CH_2) 2.6–3.1 (br s, ex, 7-OH), 3.30 (2 H, dt, *J* 6, 1.5, OCH_2), 3.72 (3 H, s, OCH_3), 4.3–4.7 (1 H, m, 2-H), 4.8–5.15 (2 H, m, CH=CH_2), 5.65–6.2 (1 H, m, C*H*=CH_2) and 6.19 (1 H, s, ArH); δ_C[20 MHz; $(CD_3)_2SO$] 20.4 (q), 26.6 (t), 45.2 (t), 55.3 (q), 73.4 (d), 92.6 (d), 104.5 (s), 105.5 (s), 114.2 (t), 136.6 (d), 159.9 (s), 161.7 (s) and 188.5 (s); *m/z* (%) 248 (M^+, 100), 219 (34), 191 (28), 149 (51) and 148 (51).

Also recovered and initially mistaken (on the basis of TLC) for the starting material with which it co-chromatographed, was an unexpected product (90 mg) tentatively identified by ^1H NMR spectroscopy as *5-methoxy-2,8-dimethyl-2,3,8,9-tetrahydrofuro*[2,3-h]-1-*benzopyran-4-one* **26** (mixture of diastereoisomers); ν_{max}(KBr)/cm^{-1} 1671s, 1623s, 1605sh s, 1595sh s and 1131m; δ_H(200 MHz; $CDCl_3$) 1.41 (3 H, d, *J* 6.3, 2-CH_3), 1.43 (3 H, pair of d, Δν 1.1, *J* 6.3, 8-CH_3), 2.54 (2 H, AB of ABX, 3-H_2), 2.64 (1 H, pair of dd, Δν 2.5, *J* 7.3, 15.0, 9-H), 3.18 (1 H, pair of dd, Δν 1.4, *J* 9.0, 15.0, 9-H), 3.81 (3 H, s, OCH_3), 4.4–4.6 (1 H, m, 2-H), 4.9–5.1 (1 H, m, 8-H) and 5.98 (1 H, s, 6-H).

8-Allyl-7-benzyloxy-5-methoxy-2-methylchroman-4-one **12**.—The chroman-4-one **11** (52 mg, 0.21 mmol), benzyl bromide (0.030 cm^3, 43 mg, 0.25 mmol) and anhydrous K_2CO_3 (100 mg) were stirred and heated together in dry purified acetone (15 cm^3) under reflux. The progress of the reaction was followed by analytical TLC, with acetone–chloroform (20:80) as developer (product at R_f 0.70; starting material at R_f 0.37). After 14 h the flask was cooled and the insoluble inorganic salts were filtered off and washed with a little acetone. The filtrate and washings were reduced to a small volume, taken up in ethyl acetate (50 cm^3), washed with water (3 × 20 cm^3) and dried ($MgSO_4$) to yield, on evaporation of the solvent, a pale brown oil containing benzyl bromide. Preparative TLC, with acetone–chloroform (10:90) as developer, gave on elution (ethyl acetate) of the major band at R_f 0.6, the *title compound* **12** (71 mg, 0.21 mmol, 100%) as a very pale yellow gum. Recrystallisation from diethyl ether gave white needles, m.p. 114.5–116 °C (Found: C, 74.7; H, 6.6. $C_{21}H_{22}O_4$ requires C, 74.54; H, 6.55%); λ_{max}(MeOH)/nm (log ε) 316sh (3.76), 284 (4.37, 246 (4.30) and 215 (4.52); ν_{max}(KBr)/cm^{-1} 1665s, 1575m, 1345m, 1273m and 1126s; δ_H(200 MHz; $CDCl_3$), 1.43 (3 H, d, *J* 6.3, CCH_3), 2.56 (2 H, AB of ABX, 3-CH_2), 3.36 (2 H, dt, *J* 6.3, 1.4, 8-CH_2), 3.83 (3 H, s, OCH_3), 4.35–4.55 (1 H, m, 2-H), 4.85–5.05 (2 H, m, CH=CH_2), 5.12 (2 H, s, OCH_2), 5.90 (1 H, ddt, *J* 17.0, 10.0, 6.3, C*H*=CH_2), 6.12 (1 H, s, ArH) and 7.25–7.45 (5 H, m, C_6H_5); δ_C(20 MHz; $CDCl_3$) 20.5 (q), 26.8 (t), 45.5 (t), 55.7 (q), 70.0 (t), 73.4 (d), 89.6 (d), 105.8 (s), 108.4 (s), 114.0 (t), 126.8 (d), 127.9 (d), 128.4 (d), 128.4 (d), 136.2 (s), 136.2 (d), 160.5 (s), 161.3 (s), 161.9 (s) and 190.2 (s); *m/z* (%) 338 (M^+, 29), 247 (12), 205 (11) and 91 (100).

7-Benzyloxy-8-(2′,3′-dihydroxypropyl)-5-methoxy-2-methylchroman-4-one **13**.—To an ice-cold solution of OsO_4 (179 mg, 0.70 mmol) in dry pyridine (2 cm^3), stirred under a dry N_2 atmosphere, was added an ice-cold solution of the chroman-4-one **12** (228 mg, 0.675 mmol) in dry pyridine (4 cm^3). The mixture rapidly darkened and was allowed to reach room temperature. Analytical TLC with chloroform–methanol (96:4) as developer, was used to follow the reaction. After 2 h no alkene (R_f 0.60) remained. A solution of $Na_2S_2O_5$ (282 mg, 1.48 mmol) in water (2 cm^3) was added and stirring was continued overnight. The flask contents were taken up in water (60 cm^3) and extracted with ethyl acetate (3 × 20 cm^3). The combined organic phases were dried ($MgSO_4$) and the solvent was evaporated to yield the *title compound* **13** (mixture of diastereoisomers) as an off-white solid (232 mg, 0.632 mmol, 94%). Recrystallisation from ethyl acetate gave rosettes of needles, m.p. 150.5–152 °C (Found: M^+, 372.152; $C_{21}H_{24}O_6$ requires *M*, 372.157); λ_{max}(MeOH)/nm (log ε) 315sh (3.75), 285 (4.35), 235sh (4.29) and 215 (4.60); ν_{max}(KBr)/cm^{-1} 3360m br, 1678s, 1602s, 1380s, 1351m and 1126s; δ_H(360 MHz; $CDCl_3$) 1.45 (3 H, pair of d, Δν 0.6, *J* 6.3, CCH_3), 2.0–2.5 (br s, ex, OH), 2.57 (2 H, AB of ABX, 3-CH_2), 2.77–2.93 (2 H, pair, Δν 6.5, of AB of ABX, 16 lines, J_{AB} 13.5, 8-CH_2), 3.40–3.56 (2 H, pair, Δν 2.6, of AB of ABX, 14 lines, J_{AB} 11.5, CH_2OH), 3.81–3.92 (1 H, m, C*H*OH), 3.83 (3 H, s, OCH_3)$_4$, 4.42–4.53 (1 H, m, 2-H), 5.12 (2 H, s, PhCH_2), 6.14 (1 H, s, 6-H) and 7.29–7.42 (5 H, m, C_6H_5); δ_C(20 MHz; $CDCl_3$) 20.5 (q), 26.6 (t), 45.5 (t), 55.8 (q), 65.8 (t). 70.4 (t), 71.7 (d), 73.8 (d), 89.9 (d), 105.9 (s), 106.1 (s), 127.1 (d), 127.1 (d), 128.3 (d), 128.7 (d), 128.7 (d), 136.6 (s), 160.9 (s), 161.5 (s), 162.3 (s) and 189.8 (s); *m/z* 372 M^+, 16), 311 (31), 221 (11), 91 (100) and 43 (56).

7-Benzyloxy-8-(formylmethyl)-5-methoxy-2-methylchroman-4-one **14**.—(*a*) To a solution of the chroman-4-one **13** (160 mg, 0.430 mmol) in methanol (7 cm^3) was added a solution of $NaIO_4$ (109 mg, 0.510 mmol) in water (7 cm^3). The mixture became slightly clouded and was stirred at room temperature for 15 h. Analytical TLC, with methanol–chloroform (4:96) as developer (product R_f 0.45, diol R_f 0.30), indicated that the reaction was complete. Water (50 cm^3) was added and the total was extracted with ethyl acetate (5 × 30 cm^3). The extract was

dried ($MgSO_4$) and the solvent was removed under reduced pressure to yield the *title compound* **14** (161 mg, 0.474 mmol, 110%) as a white, crystalline mass. A single recrystallisation from ethyl acetate–light petroleum (b.p. 40–60 °C) gave, in small yield, irregular white crystals (40 mg), m.p. 123–127 °C. Further attempts at recrystallisation resulted in decomposition and the compound also proved fairly unstable to preparative TLC.

(*b*) *7-Benzyloxy-8-(2′-hydroxyethyl)-5-methoxy-2-methylchroman-4-one* (LL-D253α–benzyl ether) **15** (51 mg, 0.149 mmol) dissolved in dry methylene dichloride (1 cm^3) was added to a suspension of pyridinium chlorochromate (48 mg, 0.223 mmol) in dry methylene dichloride (0.5 cm^3) and the mixture was stirred at room temperature with exclusion of moisture. The mixture slowly darkened and the reaction was monitored by analytical TLC with methanol–chloroform (4:96) as developer (product R_f 0.46, starting alcohol R_f 0.22). After 2 h, a spot at R_f 0.22 was still visible and further pyridinium chlorochromate (10 mg, 0.046 mmol) was added. At 4 h, careful examination of the TLC plate under both long (350 nm) and short (254 nm) wavelength UV light indicated that the remaining material at R_f 0.22 was not the starting alcohol. The reaction mixture was diluted with dry diethyl ether (10 cm^3) to give black insoluble material from which the supernatant liquor was decanted. The black solid was washed with further dry ether (causing it to become granular in appearance) and the combined supernatant and washings were filtered through Celite to give a clear solution which, on removal under reduced pressure of the solvents, yielded the *title compound* **14** (41 mg, 0.121 mmol, 81%) as a white crystalline solid (Found: M^+, 340.131. $C_{20}H_{20}H_5$ requires *M*, 340.131); $\lambda_{max}(CHCl_3)$/nm (log ε) 310 (3.63), 283 (4.24) and 252 (4.01); $\nu_{max}(KBr)/cm^{-1}$ 1724m, 1677s, 1602s, 1580sh m, 1154m and 1123s; δ_H(60 MHz; $CDCl_3$) 1.45 (3 H, d, *J* 6, CCH_3), 2.60 (2 H, AB of ABX, 3-CH_2), 3.67 (2 H, d, *J* 1.5, $ArCH_2$), 3.87 (3 H, s, OCH_3), 4.2–4.8 (1 H, m, 2-H), 5.14 (2 H, s, OCH_2–), 6.18 (1 H, s, Ar*H*), 7.36 (5 H, s, C_6H_5) and 9.60 (1 H, t, *J* 1.5, CHO); δ_C(50 MHz; $CDCl_3$) 20.4 (q), 37.8 (t), 45.5 (t), 55.9 (q), 70.5 (t), 74.0 (d), 90.0 (d), 101.7 (s), 106.0 (s), 127.1 (d), 127.1 (d), 128.2 (d), 128.6 (d), 128.6 (d), 135.7 (s), 161.7 (s), 161.7 (s), 162.4 (s) 189.5 (s) and 199.4 (d); *m/z* (%) 340 (M^+, 2), 312 (11), 221 (5), 179 (19), 149 (16), 91 (76) and 43 (100).

7-Benzyloxy-8-(2′-hydroxyethyl)-5-methoxy-2-methylchroman-4-one (*LL-D253α–Benzyl Ether*) **15**.—(*a*) A solution of sodium borohydride (10 mg, 0.26 mmol) in dry ethanol (5 cm^3) was prepared (by stirring at room temperature for 1 h) and added dropwise, with stirring, at room temperature, over 20 min to a solution of chroman-4-one **14** (40 mg, 0.12 mmol) in dry tetrahydrofuran (4 cm^3) with exclusion of moisture. The progress of the reaction was followed by analytical TLC, using precoated metal strips and with methanol–chloroform (4:96) as developer (product R_f 0.43, substrate R_f 0.58), which indicated completion after the 20 min. The reaction was quenched by pouring the mixture into dilute, aqueous HCl (0.2 mol dm^{-3}; 20 cm^3) and the resulting solution was extracted with ethyl acetate (3 × 10 cm^3). After drying ($MgSO_4$) and evaporation of the solvent, the pale yellow gum (46 mg) thus obtained was purified by preparative TLC: 2 developments with methanol–chloroform (2:98). The band at R_f 0.62 was eluted (ethyl acetate) to give a clear gum (29 mg, 0.84 mmol, 72%). The *title compound* **15** prepared in this way recrystallised from ethyl acetate to give short white rods, m.p. 133–135 °C, m.p. 133.5–136 °C, and showed characteristics (MS, IR, δ_H) identical with material prepared by the benzylation of natural LL-D253α (see below).

(*b*) 7-Hydroxy-8-(2′-hydroxyethyl)-5-methoxy-2-methylchroman-4-one (LL-D253α) **6** (265 mg, 1.05 mmol), benzyl bromide (0.135 cm^3, 194 mg, 1.13 mmol) and anhydrous potassium carbonate (402 mg) in dry purified acetone (25 cm^3) were stirred and heated together under reflux for 18 h with exclusion of moisture. Analytical TLC, with methanol–chloroform (4:96) as developer (product R_f 0.30, substrate R_f 0.15) showed that no substrate remained. After cooling, the supernatant solution was decanted and the inorganic residue was washed with further acetone. The supernatant and washings were concentrated under reduced pressure to a small volume, taken up in ethyl acetate (50 cm^3) and washed with water (3 × 20 cm^3) this was then back-extracted with further ethyl acetate (2 × 20 cm^3). The combined, dried ($MgSO_4$), organic layers were concentrated under reduced pressure to give a pale yellow oil (386 mg) containing benzyl bromide and which was purified by preparative TLC, with methanol–chloroform (4:96) as developer. The major band at R_f 0.56 was eluted [methanol–ethyl acetate (2:98)] to give, on evaporation of the solvent, the *title compound* **15** (312 mg, 0.91 mmol, 87%) as a clear semi-crystalline gum. Recrystallisation of this from ethyl acetate yielded short white rods, m.p. 135–136.5 °C (Found: C, 70.1; H, 6.5. $C_{20}H_{22}O_5$ requires C, 70.17; H, 6.48%); λ_{max}(MeOH)/nm (log ε) 316sh (3.74), 284 (4.33), 234sh (4.26) and 213 (4.53); $\nu_{max}(KBr)/cm^{-1}$ 3475br m, 1654m, 1600s, 1575m and 1126m; δ_H(60 MHz; $CDCl_3$) 1.47 (3 H, d, *J* 6, CCH_3), 1.85–2.1 (br s, OH), 2.68 (2 H, AB of ABX, 3-CH_2), 2.95 (2 H, t, *J* 6, $ArCH_2$), 4.2–4.8 (1 H, m, 2-H), 5.16 (2 H, s, $PhCH_2$), 6.16 (1 H, s, ArH) and 7.40 (5 H, s, C_6H_5); δ_C(20 MHz; $CDCl_3$) 20.6 (q), 26.2 (t), 44.5 (t), 55.8 (q), 62.2 (t), 70.2 (t), 73.6 (d), 89.8 (d), 105.9 (s), 106.9 (s), 127.0 (d), 127.0 (d), 128.1 (d), 128.6 (d), 128.6 (d), 135.9 (s), 160.7 (s), 161.7 (s), 162.4 (s) and 190.1 (s); *m/z* (%), 342 (M^+, 30), 311 (37), 221 (22), 179 (10), 91 (100) and 43 (55).

7-Hydroxy-8-(2-hydroxyethyl)-5-methoxy-2-methylchroman-4-one (*LL-D253α*) **6**.—A degassed solution of chroman-4-one **15** (278 mg, 0.81 mmol) in ethyl acetate (25 cm^3, redistilled) also containing in suspension, carbon-supported palladium catalyst (Pd/C, 10:90 w/w; 50 mg) was stirred under hydrogen gas at room temperature and pressure. Precautions were taken to exclude moisture. Samples were withdrawn at intervals by syringe through a rubber septum and analysed by TLC: precoated metal strips, with methanol–chloroform (4:96) as developer, substrate R_f 0.5, product R_f 0.25. After 7.5 h, TLC indicated completion: the catalyst was filtered off, and the solvent was removed under reduced pressure. The resulting gum (221 mg) was purified by preparative TLC with methanol–chloroform (10:90) as developer, to yield starting material (24 mg, 0.070 mmol) and 7-hydroxy-8-(2-hydroxyethyl)-5-methoxy-2-methylchroman-4-one **6** [129 mg, 0.51 mmol, 63% [69%)] as a white crystalline solid. Material prepared in this way recrystallised from ethyl acetate–methanol to give white needles, m.p. 189–191 °C, and showed characteristics (MS, IR, δ_H, TLC) identical with natural LL-D253α.

Crotonyl Chloride.—Crotonic acid (30 g, 0.35 mol) and thionyl chloride (57 g, 0.48 mol) in dry, light petroleum (b.p. 40–60 °C) (300 cm^3) were heated together under gentle reflux for 4 h with exclusion of moisture. A large volume of HCl gas was evolved. The bulk of the solvent was removed under reduced pressure and the concentrated product was distilled through a short Vigreux column to give crotonyl chloride (27.7 g, 0.265 mol, 76%) as a clear liquid, b.p. 124–126 °C at 760 mmHg (lit.,[47] 124–126 °C); δ_H(60 MHz; $CDCl_3$) 2.03 (3 H, dd, *J* 7, 1.5, $CHCH_3$), 6.10 (1 H, dq, *J* 15, 1.5, COCH) and 7.25 (1 H, dq, *J* 15, 7, $CHCH_3$).

3,5-Dimethoxyphenyl Crotonate **16**.—3,5-Dimethoxyphenol (10.00 g, 64.9 mmol) and metallic magnesium (turnings, 0.31 g) were stirred and heated together under reflux in dry benzene (30

cm^3) with exclusion of moisture. Crotonyl chloride (7.0 g, 67.0 mmol) was added dropwise over 1 h resulting in the copious evolution of HCl gas. A small quantity of red solid formed as heating was continued. After 15 h the mixture was allowed to cool. The solution was decanted from the magnesium turnings, diluted with further benzene (100 cm^3), washed with 1% w/v aqueous sodium hydroxide (3 × 50 cm^3) and water (3 × 50 cm^3), dried ($CaCl_2$) and concentrated under reduced pressure to give the *ester* **16** as a pale yellow oil (14 g). This was distilled under reduced pressure of dry nitrogen through a short Vigreux column: the fraction boiling in the range 138–141 °C (at 0.7 mmHg) was collected as a pale yellow, pleasant smelling oil (11.19 g, 50.4 mmol, 78%) which solidified on prolonged storage in a cold room. Exposure to air or light resulted in gradual darkening of the product (Found: M^+, 222.088. $C_{12}H_{14}O_4$ requires *M*, 222.089); λ_{max}(MeOH)/nm (log ε) 269 (3.27) and 213 (4.32); ν_{max}(neat)/cm^{-1} 1740s, 1615s, 1478m, 1156s and 1598sh, s; δ_H(60 MHz; $CDCl_3$) 1.98 (3 H, dd, *J* 7, 1.5, $CHCH_3$), 3.81 (6 H, s, 2 × OCH_3), 6.08 (1 H, dq, *J* 15, 1.5, COCH), 6.38 (3 H, s, 3 × ArH) and 7.27 (1 H, dq, *J* 15, 7, $CHCH_3$); δ_C(50 MHz; $CDCl_3$) 17.8 (q), 55.2 (q), 98.1 (d), 100.2 (d), 100.2 (d), 122.0 (d), 146.5 (d), 152.3 (s), 161.0 (s) and 164.3 (s); *m/z* (%), 222 (M^+, 47), 194 (5), 154 (90), 125 (19), 69 (100) and 41 (38).

5,7-*Dimethoxy*-2-*methylchroman*-4-*one* **17**.—The crotonate **16** (2.02 g, 9.10 mmol) in benzene (200 cm^3) and 10% w/v aqueous sodium hydroxide (50 cm^3) were irradiated together overnight in a Pyrex photochemical reaction vessel, fitted with a quartz, water-cooled, immersion well and a 400 W, low-pressure, mercury lamp. The two solutions were mixed by the passage of benzene-saturated nitrogen through a glass sinter in the base of the vessel. The reaction did not go to completion: analytical TLC, with acetone–chloroform (5:95) as developer, showed the presence of both starting material (R_f 0.64) and product (R_f 0.36). After three such identical procedures, the benzene component of the three combined reaction mixtures was separated and the basic layer was extracted with further benzene (2 × 200 cm^3). The combined benzene layers were washed with water (2 × 200 cm^3), dried ($CaCl_2$) and concentrated under reduced pressure to give a yellow gum (3.3 g) which was purified by flash chromatography with diethyl ether as eluent. On the basis of TLC, fractions 8–16 were combined and concentrated to give 5,7-dimethoxy-2-methylchroman-4-one **17** as a clear gum (1.28 g, 5.77 mmol, 21%) which crystallised, with time, to a white mass. Recrystallisation from ether gave rosettes of rods, m.p. 80–80.5 °C (lit.,[48] 77–79 °C); ν_{max}(KBr)/cm^{-1} 1675s, 1609s, 1572m, 1465m and 808m; δ_H(60 MHz; $CDCl_3$) 1.45 (3 H, d, *J* 6, CCH_3), 2.58 (2 H, AB of ABX, 3-CH_2), 3.78 (3 H, s, OCH_3), 3.84 (3 H, s, OCH_3), 4.2–4.7 (1 H, m, 2-H) and 6.00 (2 H, s, 2 × ArH); *m/z* (%), 222 (M^+, 93), 193 (16), 180 (100), 152 (28) and 137 (28).

5-*Hydroxy*-7-*methoxy*-2-*methylchroman*-4-*one* **18**.—To a solution of the chroman-4-one **17** (1.28 g, 5.74 mmol) in dry methylene dichloride (50 cm^3), at −78 °C, was added boron trichloride (2 cm^3, 2.9 g, 25 mmol), also previously chilled to −78 °C. A dark orange colouration developed immediately. The flask was sealed and left at room temperature for 30 min with occasional agitation. After rechilling, the flask was opened and attached to a rotary evaporator (no heat applied) for 30 min to remove the excess of BCl_3. The dark solution was then diluted (to 100 cm^3) with further methylene dichloride, washed with water (4 × 30 cm^3) and dried ($MgSO_4$). Solvent was then removed by gentle evaporation under reduced pressure (no heat applied) to yield the *title compound* **18** (1.15 g, 5.53 mmol, 96%) as a translucent, slightly green gum, pure by ^1H NMR which was stored in the dark under nitrogen. On prolonged exposure to air, or on attempts to crystallise the gum, the green colour intensified markedly. Recrystallisation from ethyl acetate–hexane gave dark-green crystalline lumps which, melted sharply, m.p. 86.5–87.5 °C (sublim.) to a colourless melt. Sublimation (80 °C at 0.2 mmHg) gave the product as white needles, m.p. 87–88 °C (sublim). (Found: C, 63.3; H, 5.8. $C_{11}H_{12}O_4$ requires C, 63.46; H, 5.81%); λ_{max}(MeOH)/nm (log ε), 322 (3.46), 296 (4.24), 226sh (4.15) and 213 (4.29); ν_{max}(KBr)/cm^{-1} 1640br s, 1580s, 1304m, 1290m, 1211s, 1154s; δ_H(60 MHz; $CDCl_3$) 1.50 (3 H, d, *J* 6, CCH_3), 2.62 (2 H, AB of ABX, 3-CH_2), 3.79 (3 H, s, O-CH_3), 4.3–4.8 (1 H, m, 2-H), 5.97 (2 H, AB, *J* 2.5, 2 × ArH) and 12.13 (1 H, s, ArOH); δ_C(50 MHz; $CDCl_3$) 20.6 (q), 43.3 (t), 55.4 (q), 73.8 (d), 93.8 (d), 94.7 (d), 103.0 (s), 162.9 (s), 164.1 (s), 167.8 (s) and 196.0 (s); *m/z* (%) 208 (M^+, 100), 193 (31), 167 (46), 166 (100), 138 (44) and 95 (29).

5-*Allyloxy*-5-*methoxy*-2-*methylchroman*-4-*one* **19**.—(*a*) The chroman-4-one **8** (1.002 g, 5.16 mmol), methyl iodide (0.32 cm^3, 0.730 g, 5.14 mmol) and anhydrous potassium carbonate (3.01 g) were heated and stirred together under reflux in dry purified acetone (100 cm^3). The progress of the reaction was monitored by analytical TLC, with acetone–chloroform (20:80) as developer. After 17 h no starting material (R_f 0.50) was present and one major product was indicated (R_f 0.66). Allyl bromide (2.2 cm^3, 3.12 g, 25.8 mmol) was added and heating was continued. At 23 h further K_2CO_3 (3.00 g) was added as the second reaction (giving one major product at R_f 0.50) was proceeding only slowly. The reaction mixture was allowed to cool for 72 h.

The inorganic salts were filtered off and washed with acetone. The combined filtrate and washings were concentrated under reduced pressure to give a semicrystalline gum. This was taken up in ethyl acetate (100 cm^3) and the solution washed with water (1 × 100 cm^3, 3 × 50 cm^3) and dried ($MgSO_4$). Removal of the solvent under reduced pressure yielded a brown gum, the constituents of which were separated by preparative TLC with diethyl ether as developer. The band at R_f 0.8 was eluted (ethyl acetate) and afforded the *title compound* **19** (790 mg, 3.19 mmol, 62%) as a pale brown crystalline solid. Recrystallisation from diethyl ether–hexane yielded white needles, m.p. 60.5–61 °C.

(*b*) This material was also prepared, also in 62% yield (using the same reagents, conditions and isolation procedure as for the second reaction of the above sequence), from the chroman-4-one **18** (Found: C, 67.9; H, 6.5. $C_{14}H_{16}O_4$ requires C, 67.73; H, 6.50%); λ_{max}(MeOH)/nm (log ε), 310sh (3.62), 280 (4.22), 225 (4.26) and 212 (4.28); ν_{max}(KBr)/cm^{-1} 1680s, 1611s, 1573m and 808m; δ_H(200 MHz; $CDCl_3$) 1.42 (3 H, d, *J* 6.2, CCH_3), 2.46–2.65 (2 H, AB of ABX, 3-CH_2), 3.76 (3 H, s, OCH_3), 4.38–4.58 (1 H, m, 2-H), 4.53 (2 H, dt, *J* 4.7, 1.7, $ArCH_2$), 5.28 (1 H, dm, *J* 10.6, CH=C*H cis*), 5.60 (1 H, dm, *J* 17.1, CH=C*H trans*), 5.92–6.14 (1 H, m, $CH{=}CH_2$) and 6.00 (2 H, AB, 2 × ArH); δ_C(20 MHz; $CDCl_3$) 20.4 (q), 45.4 (t), 55.1 (q), 68.9 (t), 73.5 (d), 93.1 (d), 93.5 (d), 105.7 (s), 117.0 (t), 131.9 (d), 160.6 (s), 164.6 (s), 165.2 (s) and 188.9 (s); *m/z* (%), 248 (M^+, 100), 233 (34), 219 (45), 150 (69) and 41 (94).

6-*Allyl*-5-*hydroxy*-7-*methoxy*-2-*methylchroman*-4-*one* **20** *and* 8-*Allyl*-5-*hydroxy*-7-*methoxy*-2-*methylchroman*-4-*one* **21**.—The chroman-4-one **19** (902 mg, 3.64 mmol), sealed *in vacuo* (0.1 mmHg) in a strong Pyrex tube (8 mm i.d. × 10 cm), was heated (200 °C) for 25 min to give a brown gum the ^1H NMR spectrum of which indicated that no allyl ether remained and that two major products had been formed. The products were separated by preparative TLC with ethyl acetate–light petroleum (b.p. 30–40 °C) (6:94) as developer (three passes per plate). The slightly more polar band (R_f 0.44) was eluted (chloroform) to give the chroman-4-one **20** (417 mg, 1.68 mmol, 46%) as a pale yellow gum. Recrystallisation of this from diethyl ether–light petrol-

eum (b.p. 30–40 °C) yielded yellow crystals which, on sublimation (75 °C at 0.05 mmHg), became white needles, m.p. 61–64 °C (Found: C, 67.5; H, 6.75. $C_{14}H_{16}O_4$ requires C, 67.73; H, 6.50%); λ_{max}(MeOH)/nm (log ε), 331 (3.46), 288 (4.28), 228sh (4.27), 214 (4.38) and 205sh (4.34); ν_{max}(KBr)/cm^{-1} 1647s, 1619s, 1576m and 1299s; δ_H(80 MHz; $CDCl_3$) 1.47 (3 H, d, *J* 6.3, CHCH_3), 2.43–2.90 (2 H, Ab of ABX, J_{AB} 17.1, 3-CH_2), 3.28 (2 H, dt, *J* 6.0, 1.5, ArCH_2), 3.81 (3 H, s, OCH_3), 4.28–4.75 (1 H, m, 2-H), 4.80–5.15 (2 H, m, CH=CH_2), 5.65–6.18 (1 H, m, C*H*=CH_2), 5.99 (1 H, s, ArH) and 12.07 (1 H, s, ArOH); δ_C(50 MHz; $CDCl_3$) 20.7 (q), 25.9 (t), 43.4 (t), 55.7 (q), 73.9 (d), 90.6 (d), 102.8 (s), 107.9 (s), 114.0 (t), 136.2 (d), 160.4 (s), 161.8 (s), 165.4 (s) and 196.1 (s); *m*/*z* (%), 248 (100), 233 (41), 221 (18), 205 (15), 206 (18), 179 (18), 178 (20) and 69 (16).

Elution (chloroform) of the less polar band (R_f 0.53) gave the chroman-4-one **21** (224 mg, 0.90 mmol, 25%) as a white crystalline solid. Recrystallisation from ether–hexane gave white needles, m.p. 76.5–77.5 °C (sublim.). Sublimation (75 °C at 2.5 mmHg) raised the m.p. to 77–78 °C (sublim.) (Found: C, 67.5; H, 6.7. $C_{14}H_{16}O_4$ requires C, 67.73; H, 6.50%); λ_{max}(MeOH)/nm (log ε) 334 (3.51), 289 (4.24), 236sh (4.09) and 214 (4.35); ν_{max}(KBr)/cm^{-1} 1635s, 1585m, 1538m, 1304m, 1206m and 1156m; δ_H(80 MHz; $CDCl_3$) 1.47 (3 H, d, *J* 6.3, CHCH_3), 2.44–2.88 (2 H, AB of ABX, J_{AB} 17, 3-CH_2), 3.25 (2 H, dt, *J* 6.1, 1.5, ArCH_2), 3.83 (3 H, s, OCH_3), 4.19–4.74 (1 H, m, 2-H), 4.78–5.09 (2 H, m, CH=CH_2), 5.59–6.13 (1 H, m, C*H*=CH_2), 6.04 (1 H, s, ArH) and 12.14 (1 H, s, ArOH); δ_C(50 MHz; $CDCl_3$) 20.6 (q), 26.4 (t), 43.3 (t), 55.7 (q), 73.6 (d), 92.1 (d), 102.8 (s), 106.9 (s), 113.9 (t), 136.4 (d), 159.2 (s), 162.8 (s), 165.5 (s) and 196.6 (s); *m*/*z* 248 (M^+, 100), 233 (14), 221 (19), 207 (11), 179 (19) and 178 (35).

This pyrolysis was also carried out on a smaller scale (50 mg) heating (200 °C) for 15 min. The vacuum (0.2 mmHg) was maintained throughout heating on this occasion. A ^{1}H NMR spectrum indicated that one product had been formed, in quantitative yield, and analytical TLC showed that this was the more polar of the two rearrangement products recorded above.

6-(2′,3′-*Dihydroxypropyl*)-5-*hydroxy*-7-*methoxy*-2-*methylchroman*-4-*one* **22**.—To an ice-cold solution of osmium tetroxide (49 mg, 0.193 mmol) in dry pyridine (1 cm^3), stirred under a dry nitrogen atmosphere, was added an ice-cold solution of the chroman-4-one **20** (47 mg, 0.190 mmol) in pyridine (2 cm^3). The mixture rapidly darkened and was stirred at room temperature for 90 min, after which time analytical TLC, with acetone-chloroform (5:95) as developer, showed that no alkene (R_f 0.35) remained. One major product (R_f 0.19), presumably the osmate ester, was present. A solution of sodium metabisulfite (80 mg, 0.42 mmol) in water (1 cm^3) was added; stirring was continued for a further 2 h. The mixture lost its dark opaque appearance to form a translucent orange solution above a dark brown solid. Water (20 cm^3) was added and the resulting solution was extracted with ethyl acetate (3 × 10 cm^3). The combined organic phases were dried ($MgSO_4$) and the solvents were removed under reduced pressure (the pyridine was co-distilled with carbon tetrachloride) to yield the title compound **22** (mixture of diastereoisomers) as a white crystalline solid. Recrystallisation from chloroform gave white needles, m.p. 149–152 °C (Found: M^+, 282.1085; $C_{14}H_{16}O_6$ requires *M*, 282.1103); λ_{max}(MeOH)/nm (log ε) 332 (3.39), 287 (4.19) and 215 (4.31); ν_{max}(KBr)/cm^{-1} 3350br m, 1641s, 1296s and 1213m; δ_H(360 MHz; $CDCl_3$) 1.49 (3 H, d, *J* 6.3, CHCH_3), 1.59 (br s, ex, OH), 2.38 (br, t, *J* 6, ex, OH), 2.49 (br, d, *J* 6, ex, OH), 2.58–2.73 (2 H, AB of ABX, J_{AB} 17.1, 3-CH_2), 2.76–2.87 (2 H, m, 11 lines, ArCH_2), 3.43–3.60 (2 H, br m, sharpened by D_2O to 16 lines, CH_2OH), 3.84 (3 H, s, OCH_3), 3.82–3.93 (1 H, m, C*H*OH), 4.49–4.61 (1 H, m, 12 lines, 2-CH), 6.03 (1 H, s, ArH) and 12.38 (1 H, 'd', ex, Ar–OH); δ_C(50 MHz; $CDCl_3$) 20.6 (q), 25.7 (t), 43.2 (t), 55.8 (q), 65.8 (t), 71.7 (d), 74.0 (d), 91.0 (d), 102.7 (s), 1.57 (s), 160.6 (s), 162.1 (s), 165.6 (s) and 196.3 (s); *m*/*z* (%) 282 (M^+, 12), 251 (14), 221 (100), 179 (48) and 69 (16).

5-*Hydroxy*-7-*methoxy*-2-*methyl*-6-(2′-*oxoethyl*)*chroman*-4-*one* **24**.—The chroman-4-one **22** (48 mg, 0.17 mmol), dissolved in methanol (2 cm^3), was added to a solution of sodium periodate (43 mg, 0.20 mmol) in water (1 cm^3) to form a cloudy suspension. This was stirred at room temperature for 17 h after which time analytical TLC with acetone–chloroform (5:95) as developer, showed that no diol (R_f 0.06) remained and one product (R_f 0.62) was present. After dilution with water (40 cm^3), the reaction mixture was extracted with ethyl acetate (4 × 10 cm^3). The extract was dried ($MgSO_4$) and concentrated under reduced pressure to give the title compound **24** as an off-white crystalline mass (42 mg, 0.17 mmol, 100%). Recrystallisation from ethyl acetate–hexane yielded fine white needles, m.p. 97–99.5 °C (Found: M^+, 250.0837. $C_{13}H_{14}O_5$ requires *M*, 250.0841); λ_{max}($CHCl_3$)/nm (log ε) 330 (3.44), 289 (4.25) and 241 (3.80); ν_{max}(KBr)/cm^{-1} 1726s, 1640s, 1577m, 1298s and 1209s; δ_H(200 MHz; $CDCl_3$) 1.48 (3 H, d, *J* 6.3, C–CH_3), 2.52–2.75 (2 H, AB of ABX, J_{AB} 17.1, 3-CH_2), 3.58 (2 H, d, *J* 1.8, ArCH_2), 3.79 (3 H, s, O–CH_3), 4.53 (1 H, m, 2-H), 6.02 (1 H, s, ArH), 9.59 (1 H, t, *J* 1.7, CH_2C*H*O) and 12.13 (1 H, s, ArOH); δ_C(50 MHz; $CDCl_3$) 20.6 (q), 36.9 (t), 55.8 (q), 74.0 (d), 90.7 (d), 100.9 (s), 102.7 (s), 160.9 (s), 162.7 (s), 165.5 (s), 191.1 (s) and 199.6 (d); *m*/*z* (%) 250 (M^+, 18), 222 (75), 221 (100) and 179 (82).

5-*Hydroxy*-6-(2-*hydroxyethyl*)-7-*methoxy*-2-*methylchroman*-4-*one* **1**.—This compound was prepared in exactly the same way as was LL-D253α–benzyl ether **15**, by borohydride reduction of the chroman-4-one **24**. Preparative TLC of the crude extract, with acetone–chloroform (5:95) as developer, gave, on elution (ethyl acetate) of the band at R_f 0.37, the required *alcohol* **1** as a white solid (72%). Recrystallisation from ethyl acetate–hexane gave white needles, m.p. 136–137 °C (sublim.) (Found: M^+, 252.0095. $C_{13}H_{16}O_5$ requires *M*, 252.0998); λ_{max}(MeOH)/nm (log ε), 332 (3.41), 288 (4.22), 227sh (4.20) and 215 (4.32); ν_{max}(KBr)/cm^{-1} 3320br m, 1648s, 1624s, 1577s and 1297s; δ_H(200 MHz; $CDCl_3$) 1.44 (3 H, d, *J* 6.3, CHCH_3), 1.94 (br s, ex, CH_2OH), 2.48–2.72 (2 H, AB of ABX, J_{AB} 17.1, 3-CH_2), 2.81 (2 H, t, *J* 6.6, ArCH_2), 3.68 (2 H, t, *J* 6.6, CH_2OH), 3.79 (3 H, s, OCH_3), 4.39–4.58 (1 H, m, 2-H), 5.98 (1 H, s, ArH) and 12.13 (1 H, s, ex, ArOH); δ_C(90 MHz; $CDCl_3$) 20.7 (q), 25.4 (t), 43.3 (t), 55.7 (q), 62.3 (t), 74.0 (d), 90.8 (d), 102.7 (s), 106.6 (2), 160.8 (s), 161.9 (s), 165.6 (s) and 196.3 (s); *m*/*z* (%) 252 (M^+, 38), 222 (28), 221 (100), 179 (57) and 69 (12).

8-(2′,3′-*Dihydroxypropyl*)-5-*hydroxy*-7-*methoxy*-2-*methylchroman*-4-*one* **23**.—To an ice-cold solution of osmium tetroxide (217 mg, 0.854 mmol) in dry pyridine (2 cm^3) stirred under a dry nitrogen atmosphere, was added an ice-cold solution of the chroman-4-one **21** (194 mg, 0.782 mmol) in dry pyridine (7 cm^3). The mixture rapidly darkened and was stirred at room temperature for 17 h. Analytical TLC, developing with acetone–chloroform (5:95), showed that no alkene (R_f 0.35) remained so a solution of sodium metabisulfite (327 mg, 1.72 mmol) in water (3 cm^3) was added. A black precipitate formed from the opaque mixture to give a translucent solution. After a further 3 h the total mixture was diluted with water (100 cm^3) and extracted with ethyl acetate (4 × 50 cm^3). The combined organic phases were washed with 2 mol dm^{-3} HCl (4 × 30 cm^3), to remove the pyridine, dried ($MgSO_4$) and concentrated under reduced pressure to give the *title compound* **23** (mixture of diastereoisomers) as a white crystalline solid (238 mg, 0.84 mmol, 107%) containing a little acetic acid. Recrystallisation from ethyl acetate–hexane gave rosettes of white needles, m.p.

164–165.5 °C (Found: M^+, 282.1087, $C_{14}H_{18}O_6$ requires *M*, 282.1103); λ_{max}(MeOH)/nm (log ε) 332 (3.43), 288 (4.16), 235sh (3.98) and 214 (4.30); ν_{max}(KBr)/cm^{-1} 3380br m, 1644s, 1626s, 1360m, 1122s; δ_H(360 MHz; $CDCl_3$) 1.51 (3 H, d, *J* 6.3, $CHCH_3$), 1.51–1.68 (br s, ex, OH), 2.04–2.21 (br s, ex, OH), 2.21–2.36 (br s, ex, OH), 2.58–2.74 (2 H, AB of ABX, 3-CH_2), 2.72–2.88 (2 H, m, 11 lines, $ArCH_2$), 3.42–3.61 (2 H, br m, sharpened by D_2O to 12 lines, CH_2OH), 3.81–3.90 (1 H, br m, sharpened by D_2O, CHOH), 3.85 (3 H, s, OCH_3), 4.47–4.60 (1 H, m, 2-H), 6.09 (1 H, s, ArH) and 12.17 (1 H, s, ex, ArOH); δ_C(50 MHz; $CDCl_3$) 20.7 (q), 26.3 (t), 55.9 (q), 65.9 (t), 71.8 (d), 74.0 (d), 92.5 (d), 102.8 (s), 104.4 (s), 159.5 (s), 163.1 (s), 165.6 (s) and 196.4 (s); *m*/*z* (%) 282 (M^+, 23), 251 (9), 222 (21), 221 (100), 209 (14), and 179 (52).

5-Hydroxy-7-methoxy-2-methyl-8-(2′-oxoethyl)chroman-4-one **25**.—8-(2′,3′-Dihydroxypropyl)-5-hydroxy-7-methoxy-2-methylchroman-2-one **23** (188 mg, 0.67 mmol), dissolved in methanol (10 cm^3), was added to a solution of sodium periodate (178 mg, 0.83 mmol) in water (5 cm^3) to form a cloudy suspension. The mixture was stirred at room temperature for 15 h, diluted with water (150 cm^3) and extracted with ethyl acetate (4 × 50 cm^3). The organic extract was dried ($MgSO_4$) and concentrated under reduced pressure to give the *title compound* **25** as pale brown plates (157 mg, 0.63 mmol, 94%). Recrystallisation from deuteriochloroform gave large, clear, square prisms, m.p. 120.5–121.5 °C. (Found: M^+, 250.0836. $C_{13}H_{14}O_5$ requires *M*, 250.0841); λ_{max}($CHCl_3$)/nm (log ε) 330 (3.43), 289 (4.17) and 241 (3.79); ν_{max}(KBr)/cm^{-1} 1715s, 1647s, 1622s, 1592m, 1208s and 1115s; δ_H(80 MHz; $CDCl_3$) 1.45 (3 H, d, *J* 6.3, $CHCH_3$), 2.63 (2 H, AB of ABX, 3-CH_2), 3.56 (2 H, d, *J* 1.8, $ArCH_2$), 3.81 (3 H, s, O–CH_3), 4.26–4.76 (1 H, m, 2-H), 6.08 (1 H, s, ArH), 9.57 (1 H, t, *J* 1.8, CHO) and 12.18 (1 H, s, ex, ArOH); δ_C(50 MHz; $CDCl_3$) 20.6 (q), 37.4 (t), 43.1 (t), 55.9 (q), 74.1 (d), 92.3 (d), 99.9 (s), 102.7 (s), 159.8 (s), 163.8 (s), 165.5 (s), 196.4 (s) and 199.5 (d); *m*/*z* (%), 250 (M^+, 16), 221 (72), 179 (100), 149 (12), 108 (14) and 69 (32).

5-Hydroxy-8-(2′-hydroxyethyl)-7-methoxy-2-methylchroman-4-one **4**.—This compound was prepared in exactly the same way as LL-D253α–benzyl ether **15**, by borohydride reduction of the chroman-4-one **25**. Preparative TLC of the crude extract with acetone–chloroform (5:95) as developer gave, on elution (ethyl acetate) of the band at R_f 0.40, the required *alcohol* **4** as a white crystalline solid in 57% yield. Recrystallisation from ethyl acetate–hexane gave white needles, m.p. 126–128.5 °C. The relatively low yield probably reflects the presence of impurities in the aldehyde which was sensitive to handling (Found: M^+, 252.1001. $C_{13}H_{16}O_5$ requires *M*, 252.0998); λ_{max}(MeOH)/nm (log ε) 333 (3.48), 288 (4.21), 233sh (4.03) and 213 (4.34); ν_{max}(KBr)/cm^{-1} 3380br m, 1648s, 1635sh s, 1357m and 1120m; δ_H(200 MHz; $CDCl_3$) 1.45 (3 H, d, *J* 6.3, $CHCH_3$), 1.95 (br s, ex, CH_2OH), 2.59 (2 H, AB of ABX, J_{AB} 17.1, 3-CH_2), 2.79 (2 H, t, *J* 6.8, $ArCH_2$), 3.65 (2 H, t, *J* 6.8, CH_2OH), 3.79 (3 H, s, OCH_3), 4.36–4.56 (1 H, m, 2-H), 6.02 (1 H, s, ArH) and 12.12 (1 H, s, ex, ArOH); δ_C(50 MHz; $CDCl_3$) 20.6 (q), 25.7 (t), 43.1 (t), 55.7 (q), 62.1 (t), 73.7 (d), 92.1 (d), 102.6 (s), 105.1 (s), 159.5 (s), 162.8 (s), 165.7 (s) and 196.5 (s); *m*/*z* (%), 252 (M^+, 27), 221 (100), 179 (58), 149 (7) and 69 (11).

6- and 8-Acetyl-5,7-dihydroxy-2-methylchroman-4-one **46** *and* **47**.—The chroman-4-one **8** (100 mg, 0.53 mmol) was stirred with acetic anhydride (5 cm^3) with the exclusion of moisture, and boron tribromide (5 cm^3) was cautiously added dropwise. This mixture was stirred at 60 °C and the reaction progress monitored by analytical TLC [acetone–chloroform (3:97)]. After 6 h the mixture was allowed to cool when it was diluted with water (20 cm^3) and extracted into ethyl acetate (× 50 cm^3 portions). The latter was dried and concentrated under reduced pressure to give a yellow solid (85 mg). Its components were separated by preparative TLC (chloroform) to give two compounds. The faster running band gave the *chroman-4-one* **46** (20 mg), m.p. 151–155 °C (Found: C, 59.9; H, 5.11. $C_{12}H_{12}O_4$ requires C, 61.0; H, 5.12%); δ_H(80 MHz; $CDCl_3$) 1.60 (3 H, d, *J* 6.3, $CHCH_3$), 2.63 (3 H, s, $COCH_3$), 2.70 (2 H, AB of ABX, 3-CH_2) 4.70 (1 H, m, 2-H), 5.99 (1 H, s, ArH), 12.66 (1 H, s, exch., ArOH) and 14.30 (1 H, s, exch., ArOH).

The slower band gave the *chroman-4-one* **45** (14 mg), m.p. 117–120 °C (Found: C, 61.0; H, 5.03. $C_{12}H_{12}O_4$ requires C, 61.0; H, 5.12%); δ_H(80 MHz; $CDCl_3$) 1.51 (3 H, d, *J* 6.3, $CHCH_3$), 2.70 (3 H, s, $COCH_3$), 2.69 (2 H, AB of ABX, 3-CH_2), 4.58 (1 H, m, 2-CH), 5.94 (1 H, s, ArH), 14.23 (1 H, s, exch., ArOH) and 14.18 (1 H, s, exch., ArOH).

7-Acetoxy-5-hydroxy-2-methylchroman-4-one **44**.—The chroman-4-one **8** (495 mg, 2.55 mmol) was stirred with acetic anhydride (283 mg, 2.77 mmol) and pyridine (5 cm^3) at ambient temperature for 6 h. The mixture was then poured on crushed ice and extracted into chloroform (2 × 100 cm^3 portions). This was washed with dilute hydrochloric acid (2 × 100 cm^3 portions), dried and concentrated under reduced pressure to give a brown solid (429 mg). This was purified by preparative TLC [acetone–chloroform (3.97)] to give white crystals (R_f 0.7) of the *title compound* **44** (430 mg, 71%). This was recrystallised from ether to give white needles, m.p. 110–112 °C (Found: C, 60.9; H, 5.22. $C_{12}H_{12}O_4$ requires C, 61.0; H, 5.11%); λ_{max}/nm (log ε) 340 (3.24) and 275 (3.83); ν_{max}(Nujol)/cm^{-1} 1754m, 1738, 1653s, 1636s, 1583s, 1290m, 1218m and 1125s; δ_H(80 MHz; $CDCl_3$) 1.43 (3 H, d, *J* 7.3, $CHCH_3$), 2.20 (3 H, s, $COCH_3$), 2.57–2.68 (2 H, AB of ABX, 3-CH_2), 4.50 (1 H, dq, *J* 7.3, 1.9, 2-CH_3), 6.15 (1 H, d, *J* 2.1, ArH), 6.18 (1 H, d, *J* 2.1, ArH) and 11.78 (1 H, s, exch., ArOH); *m*/*z* (%) 236 (M^+, 44), 194 (91), 179 (21), 153 (24) and 152 (100).

Attempted Fries Rearrangement of 7-Acetoxy-5-hydroxy-2-methylchroman-4-one.—Boron trifluoride–diethyl ether (2 cm^3) was added dropwise to the chroman-4-one **44** (53 mg, 0.22 mmol) and the mixture was stirred at 60 °C for 40 min with the exclusion of moisture. The mixture was poured on ice and then extracted into methylene dichloride (2 × 100 cm^3 portions). The resulting solution was dried and concentrated under reduced pressure to give a yellow solid which was readily soluble in chloroform. Analytical TLC [acetone–chloroform (5:95)] indicated a complex mixture of products, and the absence of both starting material and the expected product. This was confirmed from the ^{1}H NMR spectrum of the crude mixture which, however, suggested that 5,7-dihydroxy-2-methylchroman-4-one was present.

Attempted Photo-Fries Rearrangement of 7-Acetoxy-5-hydroxy-2-methylchroman-4-one **44**.—The title compound **44** (46 mg, 0.19 mmol) was dissolved in ethyl acetate (100 cm^3) in a quartz immersion well, and dry nitrogen was bubbled through the solution. This was irradiated, with water cooling, using standard photochemical apparatus (125 W) for 9 h. Removal of solvent under reduced pressure gave pale brown crystals, of starting material by analytical TLC [acetone–chloroform (3:97)]; R_f 0.6.

Attempted Photo-Fries Rearrangement of 7-Acetoxy-5-hydroxy-2-methylchroman-4-one in the Presence of Potassium Carbonate.—The title compound (48 mg, 0.20 mmol) was irradiated in ethyl acetate as described above; in addition, potassium carbonate (120 mg) was present, and the resulting suspension was stirred magnetically. After 10 h this mixture was filtered and concentrated under reduced pressure to give

a clear gum (130 mg), mainly starting material by TLC and NMR.

2-Hydroxy-4,6-dimethoxyacetophenone.—All glassware was oven-dried prior to use. Dry 2,4,6-trihydroxyacetophenone (4.295 g, 25.6 mmol), anhydrous potassium carbonate (17.65 g, 128 mmol) and dry acetone (200 cm^3) were stirred mechanically in a three-necked flask, with the exclusion of moisture. The acetone was heated under reflux, and iodomethane (8.25 cm^3, 18.8 g, 125 mmol) was added dropwise over 30 min. The reaction was monitored by preparative TLC (chloroform). After 5 h, most of the starting material [R_f 0.1; purple under UV (354 nm) irradiation] had gone, and two lower polarity spots (R_f 0.7 and 0.8; blue and purple respectively under UV irradiation) were evident. The flask's contents were allowed to cool, and were filtered. The filtrate was washed with acetone and the combined filtrate (400 cm^3) was concentrated under reduced pressure. The residue was partitioned between dilute hydrochloric acid and ethyl acetate. The latter was dried and concentrated under reduced pressure to yield a yellow solid.

Purification by flash chromatography was attempted, using a 10 mm diam. column and elution with light petroleum (b.p. 30–40 °C) containing an increasing proportion of ether. Impurities were removed, but separation of the two main components was incomplete. However partial concentration of the eluent resulted in formation of yellowy blocky prisms; filtration and slow removal of solvent yielded white needles, 2-hydroxy-4,6-dimethoxyacetophenone (3.89 g, 77%), m.p. 80–81 °C (lit.,[32] 85–88 °C); δ_H(60 MHz; $CDCl_3$) 2.60 (3 H, s, $ArCH_3$), 3.83 (3 H, s, $ArOCH_3$), 3.87 (3 H, s, $ArOCH_3$), 5.98 (1 H, d, *J* 2, ArH), 6.11 (1 H, d, *J* 2, ArH) and 14.15 (1 H, s, exch., ArOH).

Attempted Sodium–Ethanol Reduction of 2-Hydroxy-4,6-dimethoxyacetophenone.—The title compound (500 mg, 2.55 mmol) was dissolved in dry ethanol and sodium (57.5 mg, 2.5 mmol) was added. The solution was stirred under reflux for 3 h and then concentrated under reduced pressure. The residue was partitioned between dilute hydrochloric acid and ethyl acetate. The latter was dried and concentrated under reduced pressure to give a white solid which was shown to be starting material by analytical TLC and NMR.

2-Ethyl-3,5-dimethoxyphenol **47**.—Zinc (4.45 g) and mercuric chloride (220 mg) were shaken with dilute hydrochloric acid (25 cm^3) for 5 min. The aqueous solution was then decanted off, and replaced with a mixture of water and concentrated hydrochloric acid (150 cm^3 of each). 2-Hydroxy-4,6-dimethoxyacetophenone (5 g, 25.5 mmol) was added, and the suspension stirred under reflux for 4 h. Initially, not all the substrate dissolved, but as it was used up during the course of the reaction, a brown oil formed above the aqueous layer. After cooling, the supernatant liquids were decanted from any remaining zinc/mercury residues. The former were saturated with sodium chloride and extracted three times into ether (200 cm^3 total). The extract was dried and concentrated under reduced pressure to give as a yellow oil, almost pure (by NMR), 2-ethyl-3,5-dimethoxyphenol **47**. This was purified by distillation *in vacuo* to give a clear oil, b.p. 111–113 °C/2 mmHg (lit.,[49] 164 °C, 20 mmHg);ν_{max}/cm^{-1} 3420s, 1509m, 1248m, 1218m, 1202m, 1151s, 1119s, 1053m, 978m and 808m; δ_H(60 MHz; $CDCl_3$), 1.05 (3 H, t, *J* 7, CH_2CH_3), 2.52 (2 H, q, *J* 7, CH_2CH_3), 3.65 (3 H, s, OCH_3), 3.72 (3 H, s, OCH_3), 5.36 (1 H, br s, exch., ArOH), 5.97 (1 H, d, *J* 2, ArH) and 6.07 (1 H, d, *J* 2, ArH).

(4-Ethyl-3,5-dimethoxyphenyl) Crotonate **48**.—2-Ethyl-3,5-dimethoxyphenol **47** (2.0 g, 11.0 mmol) and crotonyl chloride (2.0 cm^3) were stirred under reflux with a (1 in) strip of magnesium ribbon in dry toluene (50 cm^3), with the exclusion of moisture. After 48 h, the magnesium was removed, and the organic solution was washed with water and then 2% aqueous sodium hydroxide. After drying this was concentrated under reduced pressure to give a brown oil, pure (by NMR) (4-ethyl-3,5-dimethoxyphenol) crotonate **48** (2.19 mg, 80%). This was further purified by analytical TLC [ethyl acetate–light petroleum (30:70)], to give a clear oil which slowly darkened on storage (Found: C, 65.6; H, 7.2. $C_{14}H_{18}O_4$ requires C, 65.2; H, 7.25%); λ_{max}/nm (log ε) 278 (3.39) and 239 (3.61); ν_{max}/cm^{-1} 2975m, 2947m, 2883m, 2846m, 1740s, 1656m, 1611s, 1590s, 1496m, 1455m, 1440m, 1425m, 1308m, 1292m, 1240s, 1219s, 1200s, 1151s, 1109s, 1050s, 993m, 968m and 830m; δ_H(60 MHz; $CDCl_3$) 0.93 (3 H, t, *J* 7.5, CH_2CH_3), 1.87 (3 H, dd, *J* 7, 1.5, $CHCH_3$), 2.51 (2 H, q, *J* 7.5, CH_2CH_3), 3.68 (3 H, s, OCH_3), 3.72 (3 H, s, OCH_3), 6.02 (1 H, dq, *J* 16, 1.5, COCH), 6.24 (1 H, d, *J* 2, ArH), 6.43 (1 H, d, *J* 2, ArH) and 7.18 (1 H, dq, *J* 16, 7, $CHCH_3$).

1-(3-Ethyl-2-hydroxy-4,6-dimethoxyphenyl)but-2-en-1-one **49**—(*a*). Crotonate **48** (263 mg, 1.05 mmol) and anhydrous aluminium trichloride (84 mg, 1.38 mmol) were stirred at 150 °C for 2 h with the exclusion of moisture. The resulting red gum was allowed to cool, and ice was added. The product was extracted into ethyl acetate, and the extract was dried and concentrated under reduced pressure to give a red oil. This contained [by analytical TLC; chloroform–methanol (98:2)] starting material and a product with the same properties as that obtained from the 'Magnesium-directed Friedel-Crafts reaction' described below.

(*b*) Magnesium was desiccator-dried overnight. Bromoethane was dried over magnesium sulfate, filtered and distilled from phosphorus pentoxide in the absence of moisture. All glassware was dried overnight at 120 °C. Precautions were taken to exclude moisture.

Magnesium (133 mg, 5.47 mmol) was stirred in dry ethane (15 cm^3) and bromoethane (0.38 cm^3, 0.55 g, 5.1 mmol) was added over 5 min. 2-Ethyl-3,5-dimethoxyphenol (913 mg, 5.93 mmol) in dry ether (15 cm^3) was added over 10 min, after which the ether was removed under reduced pressure at ambient temperature to give a pale yellow solid. Toluene (30 cm^3), freshly distilled from sodium was added. To the slurry was added crotonyl chloride (0.485 cm^3, 0.53 mg, 5.06 mmol) in dry toluene (7 cm^3) over 10 min, and the mixture was stirred overnight. Analytical TLC after 20 h [acetone–light petroleum (25:75)] showed one major spot, purple under UV irradiation (R_f 0.6) and others (R_f 0.55 and 0.5) corresponding to starting materials. The product was poured onto aqueous ammonium chloride and then extracted into ether (3 × 50 cm^3 portions). The yellow solution was concentrated under reduced pressure to give a brown oil, purification of which by preparative TLC [acetone–light petroleum (25:75)] yielded a yellow oil as the major component (R_f 0.75), along with some of its cyclisation product (see below). The former was crystallised from ether to give yellow needles of the *title compound* **49** (609 g, 48%), m.p. 98–105 °C (Found: C, 67.7; H, 7.29. $C_{12}H_{14}O_4$ requires C, 67.2; H, 7.25%); λ_{max}/nm (log ε) 315 (4.28), 242 (4.12) and 224sh (3.90); ν_{max}(Nujol)/cm^{-1} 1745m, 1615s, 1590s, 1147s, 1138s and 966m; δ_H(80 MHz; $CDCl_3$), 1.06 (3 H, t, *J* 7.39, $ArCH_2CH_3$), 1.94 (3 H, dd, *J* 3.83, 1.51, $CHCH_3$), 2.59 (2 H, q, *J* 7.39, CH_2CH_3), 3.86 (3 H, s, OCH_3), 3.87 (3 H, s, OCH_3), 5.93 (1 H, s, ArH), 7.04–7.32 (2 H, m, $COCH$ + $CHCH_3$) and 13.94 (1 H, exch., s, ArOH); *m/z* (%), 250 (M^+, 32), 235 (24), 182 (48), 181 (20), 167 (56) and 69 (100).

8-Ethyl-5,7-dimethoxy-2-methylchroman-4-one **50**.—The but-2-en-1-one **49** (58 mg, 0.26 mmol) was dissolved in deuteriochloroform, and shaken with a dilute solution of sodium deuteriomethoxide in deuterium oxide. Any changes were monitored by NMR; little change had occurred with 2 h and the solution was stirred overnight at ambient temperature. Its

NMR spectrum indicated the appearance of signals at 1.5 and 4.4 ppm, accompanied by diminution of signals at 1.9 and 7.0–7.3 ppm. After 94 h the product was further extracted into chloroform. This was dried and concentrated under reduced pressure to give a light-brown solid, which was purified by preparative TLC [acetone–petroleum (25:75)] to give the title compound **50** as a pale yellow solid (46 mg, 80%), m.p. 128–130 °C. This was recrystallised from ether to give white needles, m.p. 128–131 °C (Found: C, 67.3; H, 7.3. $C_{14}H_{18}O_4$ requires C, 67.2; H, 7.25%); λ_{max}/nm (log ε) 318 (3.64, 284 (4.22) and 239 (4.04); ν_{max}(Nujol)/cm^{-1} 1679s, 1573s, 1342s, 1312m, 1269s, 1211m, 1148m, 1311s, 1082m, 799m and 720m; δ_H(80 MHz; $CDCl_3$), 1.03 (3 H, t, *J* 7.36, CH_2CH_3), 1.44 (3 H, d, *J* 6.26, $CHCH_3$), 2.55 (2 H, m, 3-CH_2), 3.86 (3 H, s, $ArOCH_3$), 3.89 (3 H, s, $ArOCH_3$), 4.44 (1 H, dq, *J* 7.0, 1.6, 2-H) and 6.06 (1 H, d, ArH); *m*/*z* (%) (M^+, 96), 235 (52), 221 (33) and 193 (100).

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