Synthesis of the *Mammea* Coumarins. Part 2.[1] Experiments in the Mammea E Series and Synthesis of Mammea E/AC

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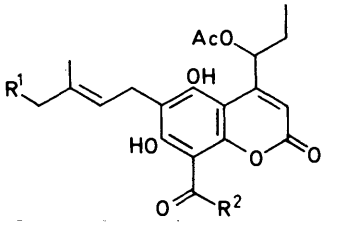
From condensations between ethyl 4-acetoxy-3-oxohexanoate and acyl phloroglucinols, 5- or 7-acyl benzo[*b*]furans (**5**) were isolated rather than the desired 4-(1-acetoxypropyl)-5,7-dihydroxy-6(or 8)-acylcoumarins. Related condensations between ethyl 4-bromo-3-oxohexanoate, or ethyl 4-chloro-3-oxobutanoate, and acyl phloroglucinols afforded either the desired 4-(1-haloalkyl)-5,7-dihydroxy-6(or 8)-acylcoumarins, or 6- or 8-acylfuro[4,3,2,-*d*,*e*][1]benzopyran-4(2*H*)-ones (**11**) by subsequent dehydrohalogenation. Attempted conversion of the 4-(1-haloalkyl)coumarins into 4-(1-acetoxyalkyl)-coumarins with sodium acetate–acetic acid gave acylbenzofurans (**5**), with silver acetate in acetonitrile gave acylfurobenzopyranones (**11**) and with tetramethylammonium acetate gave the isomeric acylfuro-benzopyranones (**13**). Allylic bromination of 6-butyryl-5,7-dimethoxy-4-propylcoumarin and conversion of the 4-(1-bromopropyl) product to a 4-(1-acetoxypropyl)coumarin, followed by a difficult demethylation and subsequent *C*-prenylation afforded mammea E/AC, a 6-acyl isomer of one of the natural 8-acyl insecticidal *Mammea* coumarins; application of this sequence to 8-butyryl-5,7-dimethoxy-4-propylcoumarin failed at the demethylation stage.

Investigations of the constituents of various parts of the insecticidal tree *Mammea americana*, especially of the seeds, have led to the isolation of some twenty 4-alkyl- or 4-aryl-5,7-dioxygenated coumarins;[2] additional members of this so-called *Mammea* coumarin group of natural products have been isolated from other plants of the Guttiferae, notably *M. africana*[3] and *M. longifolia*,[4] as well as *Mesua ferrea*[5] and *Mesua thwaitesii*,[6] so that the group includes nearly fifty compounds.[7] The remaining substituents on the coumarin nucleus are an acyl group (either 3-methylbutyryl, 2-methylbutyryl, butyryl, or 2-methylpropionyl) at C-6 or C-8, and a prenyl group (which may be oxidatively modified) or a geranyl substituent at C-8 or C-6.

The previous paper in this series[1] has described synthesis of the 4-phenyl (mammea A), 4-propyl (mammea B), and 4-pentyl (mammea C) series; thus apart from the single 4-(1-methylpropyl)coumarin, mammea D/BB from *Mesua ferrea*, the remaining targets are the important insecticidal mammea E series of 4-(1-acetoxypropyl)coumarins. The compounds mammea E/BA (**1a**), E/BB (**1b**), and either E/BC (**1c**) or E/BD (**1d**) are the insecticidal principles of *Mammea americana*,[2] and surangin B (**1e**) from *M. longifolia* also has insecticidal properties.[2] We report here our efforts to prepare these 4-(1-acetoxypropyl)coumarins, either by modification of our route to the mammea A, B, and C series, or by subsequent functionalisation of the 4-(1-propyl) position after coumarin formation, that have culminated in preparation of a 6-acyl isomer of the natural insecticides, *i.e.* mammea E/AC. The route finally developed for preparation of (**1a**, **b**, and **e**) is described in the following paper.[8]

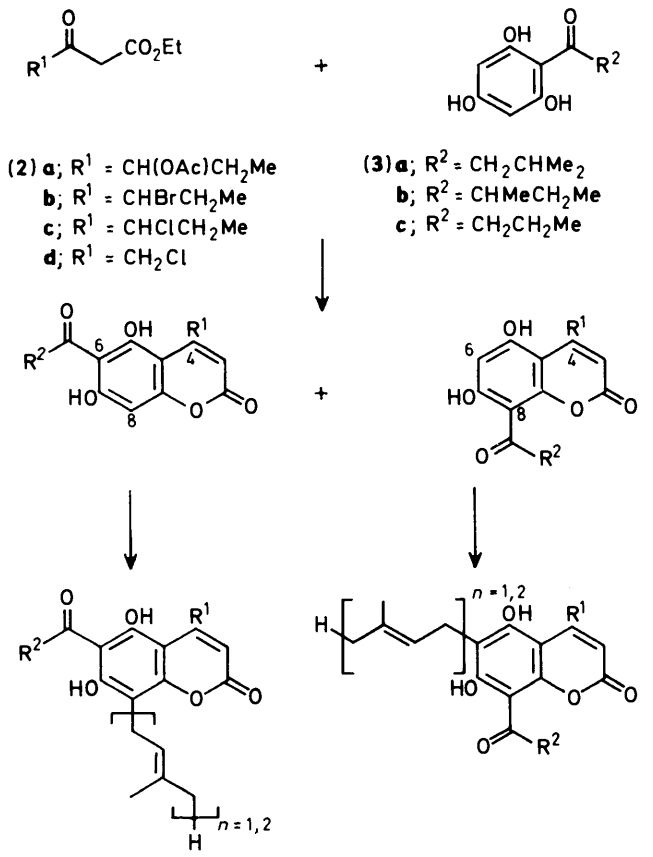


(**1**) **a**; R^1 = H, R^2 = CH_2CHMe_2
b; R^1 = H, R^2 = $CHMeCH_2Me$
c; R^1 = H, R^2 = CH_2CH_2Me
d; R^1 = H, R^2 = $CHMe_2$
e; R^1 = $CH_2CH{=}CMe_2$, R^2 = $CHMeCH_2Me$

Results and Discussion

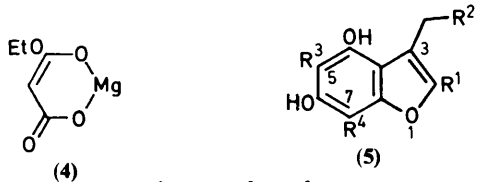
The synthetic approach developed in our laboratories to the mammea A, B, and C coumarins comprises Pechmann condensation of an appropriately substituted β-keto ester to give a separable mixture of 6- and 8-acylcoumarins that are then separately *C*-alkylated with a prenyl (or geranyl) halide (Scheme 1).[1] In order to examine this route as an approach to the mammea E coumarins, the β-keto ester 4-acetoxy-3-oxohexanoate (**2a**) was prepared from 2-acetoxybutyryl chloride. Several methods were examined, including (*a*) treatment of 2-acetoxybutyryl chloride with lithio-ethyl acetate (from ethyl acetate and lithium di-isopropylamide) or its *O*-t-butyldimethylsilyl derivative,[9] (*b*) acylation of the isopropylidene ester of malonic acid (Meldrum's acid) with 2-acetoxybutyryl chloride followed by ethanolysis,[10] and (*c*) acylation of the magnesium derivative of ethyl t-butyl malonate with the same acid chloride, followed by acid-catalysed t-butyl ester cleavage and decarboxylation.[11] All led to (**2a**) but the most reliable method on a preparative scale proved to be acylation of the magnesium complex (**4**), formed from ethyl hydrogen malonate and isopropylmagnesium bromide (2 equivs.).[12] Decarboxylation during work-up led to isolation of pure (**2a**) in 88% distilled yield based on the 2-acetoxybutyryl chloride.

Several attempted Pechmann condensations between the acetoxy β-keto ester (**2a**) and either (3-methylbutyryl)phloroglucinol (**3a**) or (2-methylbutyryl)phloroglucinol (**3b**), using as the condensing medium the 5% sulphuric acid in glacial acetic acid mixture that had been successfully employed in the mammea A, B, and C series, did not afford any coumarin material. T.l.c. examination showed that the β-keto ester had been consumed but that some unchanged acyl phoroglucinol remained. On two occasions, however, some condensation products were isolated in low yield after extensive chromatography. From a condensation between (2-methylbutyryl)-phloroglucinol (**3b**) and β-keto ester (**2a**), after removal of



Scheme 1.

starting material (**3b**) from the crude products, a mixture of two components, A and B, was isolated that was separable by h.p.l.c. Examination of the spectral properties of A showed it to be the 7-acylbenzo[*b*]furan (**5a**); in particular the ^{1}H n.m.r. spectrum had signals corresponding to a 2-methylbutyryl moiety along with a single aromatic proton, one chelated and one non-chelated hydroxy group. In addition a three-proton triplet at

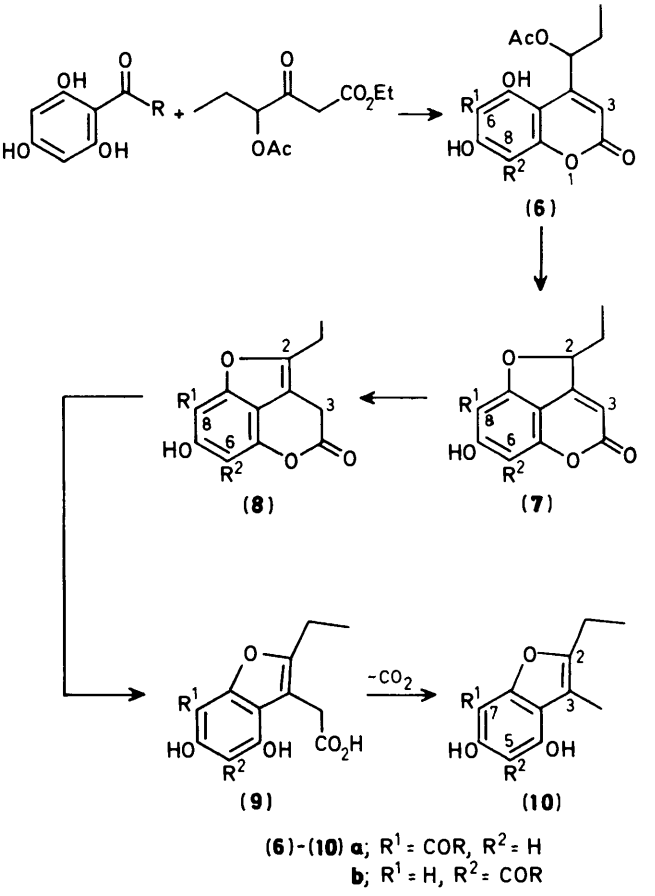


(4) (5)

a; R^1 = Et, R^2 = R^3 = H, R^4 = $COCHMeCH_2Me$
b; R^1 = Et, R^2 = CO_2Me, R^3 = H, R^4 = $COCHMeCH_2Me$
c; R^1 = Et, R^2 = CO_2H, R^3 = $COCH_2CHMe_2$, R^4 = H
d; R^1 = Et, R^2 = R^3 = H, R^4 = $COCH_2CHMe_2$
e; R^1 = R^2 = R^3 = H, R^4 = $COCH_2CH_2Me$

δ 1.3, coupled to a two-proton quartet at δ 2.75, and a three-proton singlet at δ 2.3 are consistent with a 2-ethyl-3-methylbenzofuran formulation. A negative Gibbs test confirms the location of the acyl group at C-7. Compound B had a u.v. spectrum identical to that of A, but displayed a carbonyl band at 1 710 cm^{-1} in the i.r. spectrum. The ^{1}H n.m.r. spectrum was also similar to that of A, but with the three-proton singlet at δ 2.3 replaced by a six-proton multiplet at δ 3.9 which apparently comprised a one-proton multiplet (methine proton of the acyl group) and two overlapping singlets, of two and three protons, respectively. Combined with a negative Gibbs test this is consistent with the 7-acyl-3-methoxycarbonylmethylbenzofuran structure (**5b**). The related 5-acylbenzofuran (**5c**) was isolated from a condensation between the β-keto ester (**2a**) and (3-methylbutyryl)phloroglucinol (**3a**). Benzofuran (**5c**) had an identical u.v. absorption to (**5a** and **b**), but had i.r. absorptions at 1 725 and 3 000—3 500br cm^{-1}. The ^{1}H n.m.r. spectrum indicated the presence of the 3-methylbutyryl moiety and the ethyl substituent, one chelated hydroxy group, and a broad two-proton signal corresponding to the acid and unchelated hydroxy group protons. A two-proton singlet at δ 3.8 was in accord with a carboxymethyl group and a positive Gibbs test indicated the 5-acyl substitution.

A possible pathway for the formation of these benzofurans, that encompasses the other benzofurans and related compounds described later in this paper, is outlined in Scheme 2.

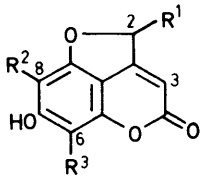


Scheme 2.

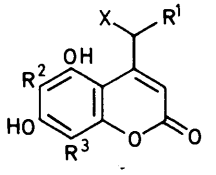
Initial formation of the desired 4-(1-acetoxypropyl) coumarins (**6a,b**) is assumed, although these materials were not isolated (the crude reaction products do show an ion of low intensity in the mass spectrum, corresponding to the molecular formula of these coumarins). Intramolecular displacement of acetate leads to the furocoumarins {furo[4,3,2-*d,e*][1]benzopyran-4(2*H*)-ones} (**7a,b**). This type of cyclisation occurs readily with 4-(1-bromopropyl) and 4-chloromethyl coumarins (see later). Acid-catalysed double-bond migration would lead to the isomeric furobenzopyran-4(3*H*)-ones (**8a,b**); this type of compound has been isolated from treatment of 4-(1-bromopropyl) and 4-chloromethyl coumarins with tetramethylammonium acetate (see later). Lactone opening by addition of water from the reaction medium affords carboxymethylbenzofurans (**9a,b**) that my undergo decarboxylation to give 3-methylbenzofurans

(**10a,b**). Formation of the ester (**5b**) is presumed to be due to contact of a carboxymethylbenzofuran with methanol during purification. This mechanistic sequence accounts for formation of both 5- and 7-acylbenzofurans, and is consistent with the benzofurans isolated from 4-(1-bromopropyl)- and 4-chloromethylcoumarins (see later), where only 7-acylbenzofurans are found to arise from 6-acylcoumarins.

The failure to achieve successful Pechmann condensations between acylphloroglucinols and the acetoxy β-keto ester led us to consider alternative γ-functionalised β-keto esters. Trials with methyl 4-hydroxy-3-oxohexanoate or ethyl 3-oxohex-4-enoate were unpromising, and our attention turned to γ-halogenated β-keto esters. Ethyl 4-bromo- and 4-chloro-3-oxohexanoate (**2b** and **c**), respectively, were prepared in high yield from the magnesium malonate complex (**4**) and 2-bromo- or 2-chlorobutyryl chloride, respectively; both these β-keto esters proved to be rather unstable liquids rapidly darkening even in the dark at 0 °C under nitrogen. Nevertheless the γ-bromo β-keto ester (**2b**) was treated with (2-methylbutyryl)-phloroglucinol (**3b**) in 5% sulphuric acid in glacial acetic acid. Chromatography of the complex mixture of products afforded not the desired 4-(1-bromopropyl)coumarins but the 8-acylfurobenzopyran-4(2*H*)-one (**11a**) together with the 6- and 8-acyl-4-propylcoumarins (**12a** and **b**), respectively; the 4-propyl-



(**11**) **a**; R^1 = Et, R^2 = $COCHMeCH_2Me$, R^3 = H
b; R^1 = Et, R^2 = $COCH_2CHMe_2$, R^3 = H
c; R^1 = R^2 = H, R^3 = $COCH_2CH_2Me$
d; R^1 = H, R^2 = $COCH_2CH_2Me$, R^3 = H
e; R^1 = Et, R^2 = $COCH_2CH_2Me$, R^3 = H



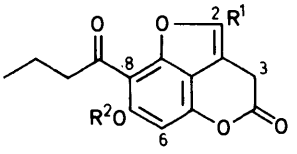
(**12**) **a**; X = H, R^1 = Et, R^2 = $COCHMeCH_2Me$, R^3 = H
b; X = H, R^1 = Et, R^2 = H, R^3 = $COCHMeCH_2Me$
c; X = Br, R^1 = Et, R^2 = $COCH_2CHMe_2$, R^3 = H
d; X = Cl, R^1 = H, R^2 = $COCH_2CH_2Me$, R^3 = H
e; X = OH, R^1 = Et, R^2 = $COCH_2CH_2Me$, R^3 = H
f; X = OH, R^1 = Et, R^2 = H, R^3 = $COCH_2CH_2Me$
g; X = OH, R^1 = Et, R^2 = R^3 = H

coumarins presumably arise from reductive debromination of an intermediate. The furobenzopyran-4(2*H*)-one probably arises from the desired 4-(1-bromopropyl)coumarins by dehydrobromination, possibly during purification. The location of the acyl group in (**11a**) was achieved by comparison of the u.v. spectrum with 6- and 8-acylfurobenzopyran-4(2*H*)-ones of known orientation (see later).

When the crude product of a condensation in 5% sulphuric acid in glacial acetic acid between (3-methylbutyryl)phloroglucinol (**3a**) and the γ-bromo β-keto ester (**2b**) was recrystallised immediately upon isolation, a small amount of 6-acyl-4-(1-bromopropyl)coumarin (**12c**) was isolated. The u.v. spectrum closely resembled those of other synthetic 6-acylcoumarins, but the base shifted spectrum resembled that of an 8-acylfurobenzopyran-4(2*H*)-one, indicating that dehydrobromination to (**11b**) occurs easily in basic solution. The remainder of the product isolated indeed proved to be the furobenzopyran-4(2*H*)-one (**11b**), with spectral properties very similar to (**11a**). An attempt was made to convert the 4-(1-bromopropyl)-coumarin (**12c**) to a 4-(1-acetoxypropyl)coumarin by treatment with sodium acetate in acetic acid, but the only product isolated was the 7-acylbenzofuran (**5d**), isomeric with (**5a**) (see above); formation of (**5d**) can be rationalised as shown in Scheme 2 following intramolecular bromide displacement to give a furobenzopyran-4(2*H*)-one.

The obvious instability of 4-(1-bromopropyl)coumarins led us to consider the corresponding chlorocoumarins; our investigations employed the stable and commercially available ethyl 4-chloro-3-oxobutanoate (**2d**) rather than the less stable (**2c**). Condensation between butyrylphloroglucinol (**3c**) and (**2d**) gave a good yield of coumarin which proved to be largely the 6-acyl-4-chloromethyl compound (**12d**) with only a low yield of the impure 8-acyl isomer being isolated. A further minor product was the 6-acylfurobenzopyran-4(2*H*)-one (**11c**), possibly indicating that the 8-acyl-4-chloromethyl coumarin is more prone to intramolecular dehydrochlorination than the 6-acylcoumarin (**12d**).

Conversion of the 4-chloromethyl coumarin (**12d**) to the corresponding 4-acetoxymethyl compound was attempted firstly by treatment with silver acetate in acetonitrile, but the product isolated was the 8-acyl furobenzopyran-4(2*H*)-one (**11d**); the spectral properties of (**11d**) and its isomer (**11c**) (see above) were distinctly different, and the u.v. spectra were sufficiently dissimilar to allow the orientation of acyl groups in other furobenzopyran-4(2*H*)-ones (see above) by comparison. As expected from our earlier finding with the 4-(1-bromopropyl)-coumarin (**12c**), treatment of the 4-chloromethyl coumarin (**12d**) with sodium acetate in acetic acid afforded a 7-acylbenzofuran (**5e**). Finally reaction of (**12d**) with tetramethylammonium acetate in dry acetone gave a high yield of the furobenzopyran-4(3*H*)-one (**13a**); presumably (**13a**) is formed



(**13**) **a**; R^1 = R^2 = H
b; R^1 = Et, R^2 = Ac

by intramolecular dehydrochlorination, with acetate as base, to a furobenzopyran-4(2*H*)-one and then double bond migration (see Scheme 2), with the anhydrous conditions precluding further transformations based on lactone ring-opening.

With the above results in hand, it was decided to abandon attempts to prepare the mammea E coumarins using a γ-functionalised β-keto ester. Our next strategy (see Scheme 3) was to attempt functionalisation of the 4-(1-propyl) position subsequent to Pechmann condensation, *i.e.* in the acyl-4-propylcoumarins whose synthesis has been described previously. The coumarin selected for initial exploration of this approach was 6-butyryl-5,7-dihydroxy-4-propylcoumarin (**14a**). It was deemed necessary to protect the hydroxy groups to avoid reaction with any substituent introduced at the 4-(1-propyl) position, so (**14a**) was first converted into the 6-butyryl-5,7-dimethoxycoumarin (**14b**) in good yield using dimethyl sulphate and potassium carbonate in acetone. Almost quantitative conversion to the corresponding 4-(1-bromopropyl) compound (**15a**) was achieved using *N*-bromosuccinimide in deoxygenated carbon tetrachloride; reaction was initiated by azo(isobutyronitrile). This bromination took a surprisingly long time (2—5 days) to reach completion, as monitored by the ^{1}H n.m.r. spectrum, and

earlier termination of the reaction was undesirable as separation of the product (**15a**) from starting material (**14b**) proved difficult. Conversion of the 4-(1-bromopropyl)coumarin (**15a**) to the 4-(1-acetoxypropyl)coumarin (**16a**) was successfully accomplished using either silver acetate in acetonitrile, sodium acetate in acetic acid, or tetramethylammonium acetate in acetone, although the latter method gave the cleanest product and the best yield.

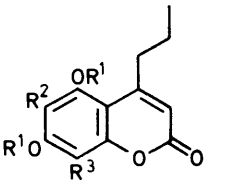
Interestingly, the 4-(1-acetoxypropyl) compound (**16a**) was obtained as suitable crystals for an *X*-ray analysis; this study, which will be presented in detail in a subsequent paper,[13] confirmed the structure of (**16a**) as formulated. The orientation of the acyl group at C-6 in the starting material (**14a**), and our assignment of structures to all the other 6- and 8-acylcoumarins synthesized in our studies on *Mammea* coumarins, based on u.v. data and the Gibbs test, are therefore substantiated.

Removal of the methyl protecting groups in (**16a**) with retention of the acetoxy function proved to be the most difficult step in the sequence. Treatment of (**16a**) with magnesium iodide–diethyl ether in benzene for 2 h afforded a monohydroxycoumarin in good yield; a positive Gibbs test showed this to be the 5-hydroxy-7-methoxycoumarin (**16b**). No trace of the 7-hydroxy-5-methoxy isomer (**16c**) was found, but a small amount of the desired dihydroxy compound (**17a**) was isolated. Extended reaction time did not lead to increased conversion to (**17a**) but instead afforded the furobenzopyran-4(2*H*)-one (**11e**) as the major product, along with a small amount of the monohydroxy coumarin (**16b**). Reaction of the dimethoxy compound (**16a**) with boron tribromide in dichloromethane at −78 °C gave, in a combined yield of 90%, a mixture of the two monohydroxycoumarins (**16b** and **c**) that could be separated by column chromatography. Similar mixtures were obtained using boron trichloride in place of the tribromide, and also using aluminium trichloride in ethanethiol. The recently reported phenylthiotrimethylsilane reagent failed to produce any demethylation.[14]

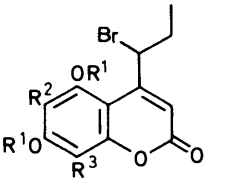
We reasoned that the failure of these reagents to remove more than one methyl group from (**16a**) was due to chelation of the Lewis acid with the acyl group at C-6 and the first liberated phenolic group, thus preventing its chelation with the remaining methoxy group which would facilitate a second demethylation. A mixture of the monohydroxycoumarins (**16b** and **c**) was therefore treated with trimethylsilyl chloride–triethylamine to silylate the phenolic group, and then with boron tribromide to afford a 64% recovery of the mixed monohydroxycoumarins for re-use and the desired dihydroxycoumarin (**17a**) in 29% yield, representing 62% from the dimethoxy coumarin (**16a**) on the basis of converted starting material. The procedure was not improved by use of t-butyldimethylsilyl chloride instead of the trimethylsilyl chloride. Conversion of the 5-hydroxy-7-methoxycoumarin (**16b**) to its acetate (**16d**), followed by treatment with boron tribromide gave only the trihydroxycoumarin (**12e**) along with recovered acetate (**16d**).

The method we have reported for the *C*-prenylation of other precursors to *Mammea* coumarins involves treatment with prenyl bromide in excess 10% aqueous potassium hydroxide at 0 °C,[1] but as expected an excess of aqueous base converted the dihydroxycoumarin (**17a**) to the trihydroxycoumarin (**12e**). If, however, (**17a**) was treated with prenyl bromide and only 2 equivalents of 5% aqueous potassium hydroxide, then formation of (**12e**) was minimised (2%) and *C*-alkylation proceeded to afford a 21% yield of mammea E/AC (**17b**), along with recovered (**17a**). Mammea E/AC is the unnatural (*i.e.* not yet isolated) 6-acyl isomer of the natural insecticidal 8-acylcoumarin mammea E/BC (**1c**), and this work represents the first synthesis of a fully substituted coumarin of the important mammea E series.[15]

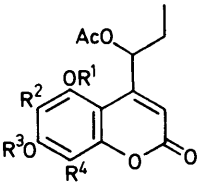
Synthesis of the naturally-occurring 8-acyl mammea E/BC



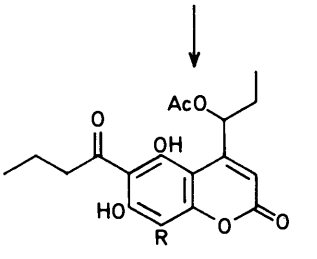
(**14**) **a**; R^1 = H, R^2 = $COCH_2CH_2Me$, R^3 = H
b; R^1 = Me, R^2 = $COCH_2CH_2Me$, R^3 = H
c; R^1 = R^2 = H, R^3 = $COCH_2CH_2Me$
d; R^1 = Me, R^2 = H, R^3 = $COCH_2CH_2Me$
e; R^1 = Ac, R^2 = $COCH_2CH_2Me$, R^3 = H



(**15**) **a**; R^1 = Me, R^2 = $COCH_2CH_2Me$, R^3 = H
b; R^1 = Me, R^2 = H, R^3 = $COCH_2CH_2Me$
c; R^1 = Ac, R^2 = $COCH_2CH_2Me$, R^3 = H



(**16**) **a**; R^1 = Me, R^2 = $COCH_2CH_2Me$, R^3 = Me, R^4 = H
b; R^1 = H, R^2 = $COCH_2CH_2Me$, R^3 = Me, R^4 = H
c; R^1 = Me, R^2 = $COCH_2CH_2Me$, R^3 = R^4 = H
d; R^1 = Ac, R^2 = $COCH_2CH_2Me$, R^3 = Me, R^4 = H
e; R^1 = Me, R^2 = H, R^3 = Me, R^4 = $COCH_2CH_2Me$
f; R^1 = Me, R^2 = R^3 = H, R^4 = $COCH_2CH_2Me$
g; R^1 = Ac, R^2 = H, R^3 = Ac, R^4 = H
h; R^1 = R^2 = R^3 = R^4 = H



(**17**) **a**; R = H
b; R = $CH_2CH{=}CMe_2$

Scheme 3.

(**1c**) was next attempted by the same route (Scheme 3). 8-Butyryl-5,7-dihydroxy-4-propylcoumarin (**14c**) was converted to the dimethoxy derivative (**14d**) with dimethyl sulphate–potassium carbonate in acetone. The coumarin (**14d**) was first brominated with *N*-bromosuccinimide in carbon tetrachloride to give (**15b**) which was then treated with tetramethylammonium acetate to afford (**16e**); all these reactions gave good yields. Once again demethylation proved difficult. Treatment of the dimethoxycoumarin (**16e**) with boron tribromide at −78 °C led exclusively to the 5-methoxy-7-hydroxycoumarin (**16f**), the selectivity presumably due to chelation of the boron tribromide to the 8-acyl substituent. This assistance is not available for demethylation at C-5, and indeed we were unable to cleave this methoxy group whilst leaving the acetoxy function intact. As expected, conversion of the monohydroxycoumarin (**16f**) to its 7-*O*-silyl ether or 7-*O*-acetate, followed by reaction with boron tribromide, served only to regenerate (**16f**) in contrast to our experience in the 6-acyl series. Treatment of (**16f**) with magnesium iodide–diethyl ether or trimethylsilyl iodide had no effect, and the only method tried that did cleave the 5-methoxy group, reaction with lithium t-butyl sulphide in HMPA at 75 °C, led to a modest yield of the trihydroxy compound (**12f**).

Alternatives to the methyl protecting groups were next considered and, after unproductive studies with benzyl and β-methoxyethoxymethyl ethers, we were prompted to investigate acetate esters as the protecting function by a report of the selective deacylation of aromatic acetates in the presence of aliphatic acetates using activated zinc.[16] Further encouragement was obtained when it was found that using this method the triacetoxycoumarin (**16g**) was converted efficiently to 4-(1-acetoxypropyl)-5,7-dihydroxycoumarin (**16h**); the triacetate (**16g**) was available by acetylation of 5,7-dihydroxy-4-(1-hydroxypropyl)coumarin (**12g**), a by-product from the Pechmann condensation of β-keto ester (**2a**) with phloroglucinol.[8] 6-Butyryl-5,7-dihydroxy-4-propylcoumarin (**14a**) was therefore converted into its diacetate derivative (**14e**), which was brominated with *N*-bromosuccinimide to give the 4-(1-bromopropyl) compound (**15c**). Unfortunately treatment of (**15c**) with tetramethylammonium acetate did not produce the corresponding 4-(1-acetoxypropyl)coumarin but instead gave the furobenzopyran-4(3*H*)-one (**13b**) in high yield [*cf.* formation of (**13a**) described earlier]; a possible rationalisation of this transformation is *via* acetate-mediated deacylation at the 5-hydroxy group followed by furan ring-closure and double bond migration (*cf.* Scheme 2).

At this point we ceased work on this route to the 8-acyl mammea E coumarins (**1a**—**e**) because of developments in another, eventually successful, approach which is described in the following paper.[8] The route of Scheme 3 is thus to date suitable for synthesis of the 6-acyl isomers of the natural *Mammea* insecticides, as exemplified by the preparation of mammea E/AC, but needs further development to be useful in the 8-acyl mammea E/B series.

Experimental

General directions are as in Part 1[1] with the following additions: ^{1}H n.m.r. spectra measured at 90 MHz were recorded on a Perkin-Elmer R32 spectrometer, and normal-phase h.p.l.c. was performed on a Waters Prep. PAK-500 silica column.

Ethyl 4-*Acetoxy*-3-*oxohexanoate* (**2a**).—To a stirred mixture of magnesium turnings (8.4 g, 0.35 mol) in dry THF (350 ml) under nitrogen was added 2-bromopropane (43.05 g, 0.35 mol) at a rate sufficient to cause the mixture to boil under reflux. After the addition was complete, the solution was heated under reflux to remove the remaining magnesium and leave a 1 M solution of isopropylmagnesium bromide in THF. This solution was added dropwise to dry ethyl hydrogen malonate (19.8 g, 150 mmol)[17] in dry dichloromethane (60 ml) stirred under nitrogen. The exothermic reaction caused the mixture to boil under reflux with rapid evolution of propane. After the addition was complete, the mixture was allowed to cool to room temperature and then further cooled in ice–salt. 2-Acetoxybutyryl chloride (9.87 g, 60 mmol) in dry dichloromethane (25 ml) was then added with stirring and the mixture allowed to warm to room temperature. The mixture was poured into cold 10% hydrochloric acid (250 ml) and, after cessation of CO_2 evolution, the solution was extracted with chloroform. The combined organic extracts were washed to basicity with saturated aqueous sodium hydrogen carbonate, and then with water, and dried ($CaCl_2$). The solvents were evaporated and the residue distilled under reduced pressure to afford *ethyl* 4-*acetoxy*-3-*oxohexanoate* (**2a**) (88%), b.p. 90—92 °C at 1 mmHg (Found: C, 55.25; H, 7.7. $C_{10}H_{16}O_5$ requires C, 55.55; H, 7.41%); $\nu_{max.}$(film) 2 950, 1 730, and 1 660 cm^{-1}; δ($CDCl_3$) 1.00 and 1.28 (each 3 H, t, *J* 7 Hz, *Me*CH_2), 1.7—2.0 (2 H, m, MeCH_2CH), 2.16 (3 H, s, MeCO), 3.52 (2 H, s, COCH_2CO), 4.20 (2 H, q, *J* 7 Hz, MeCH_2O), and 5.12 (1 H, t, *J* 7 Hz, OCHCO). The 2-acetoxybutyryl chloride used above was prepared in 84% yield from treatment of 2-acetoxybutyric acid[18] in benzene with thionyl chloride at reflux for 2 h, removal of the solvent and the excess thionyl chloride by evaporation under reduced pressure, and distillation of the residue, b.p. 75—80 °C at 25 mmHg (lit.,[18] 72 °C at 14 mmHg), $\nu_{max.}$(film) 1 790 and 1 740 cm^{-1}; δ($CDCl_3$) 1.04 (3 H, t, *J* 7 Hz, *Me*CH_2), 2.00 (2 H, m, *J* 7 Hz, MeCH_2CH), 2.16 (3 H, s, MeCO), and 5.08 (1 H, t, *J* 7 Hz, CH_2C*H*CO). The following compounds were prepared similarly:

Ethyl 4-*bromo*-3-*oxohexanoate* (**2b**). This was prepared as above from 2-bromobutyryl chloride in 80% yield, b.p. 80—90 °C at 1 mmHg (Found: M^+, 236.0068. $C_8H_{13}BrO_3$ requires *M*, 236.0049); $\nu_{max.}$(film) 2 950, 1 740, and 1 710 cm^{-1}; δ($CDCl_3$) 1.00 and 1.24 (each 3 H, t, *J* 7 Hz, *Me*CH_2), 1.7—2.2 (2 H, m, Me CH_2CH), 3.46 and 3.72 (2 H, dd, *J* 16 and 26 Hz, $COCH_2CO$), 4.10 (2 H, q, *J* 7 Hz, MeCH_2O), and 4.26 (1 H, t, *J* 7 Hz, BrCHCO). This compound discoloured rapidly, and satisfactory combustion analysis could not be obtained. The 2-bromobutyryl chloride used here was prepared as above from 2-bromobutyric acid in 79% yield and had b.p. 52—58 °C at 25 mmHg (lit.,[19] 43 °C at 12 mmHg); $\nu_{max.}$(film) 1 780 cm^{-1}; δ($CDCl_3$) 1.10 (3 H, t, *J* 7 Hz, *Me*CH_2), 2.0—2.4 (2 H, m, CH_2CH), and 4.55 (1 H, t, *J* 7 Hz, CH_2C*H*Br).

Ethyl 4-*chloro*-3-*oxohexanoate* (**2c**). This was prepared as above from 2-chlorobutyryl chloride in 83% yield, b.p. 65—75 °C at 0.8 mmHg (Found: M^+, 192.0526. $C_8H_{13}ClO_3$ requires *M*, 192.0533); $\nu_{max.}$(film) 2 950, 1 750, 1 720, and 1 660 cm^{-1}; δ($CDCl_3$) 1.04 and 1.26 (each 3 H, t, *J* 7 Hz, *Me*CH_2), 1.7—2.2 (2 H, m, MeCH_2CH), 3.54 and 3.76 (2 H, dd, *J* 16 and 20 Hz, $COCH_2CO$), 4.12 (2 H, q, *J* 7 Hz, MeCH_2O), and 4.24 (1 H, t, *J* 7 Hz, ClCHCO). This compound discoloured rapidly, and satisfactory combustion analysis could not be obtained. The 2-chlorobutyryl chloride used here was prepared as above from 2-chlorobutyric acid in 82% yield and had b.p. 128—132 °C (lit.,[20] 129—132 °C), $\nu_{max.}$(film) 1 800 cm^{-1}; δ($CDCl_3$) 1.10 (3 H, t, *J* 7 Hz, *Me*CH_2), 1.9—2.4 (2 H, m, CH_2CH), and 4.52 (1 H, t, *J* 7 Hz, CH_2C*H*Cl).

Condensation of (2-*Methylbutyryl*)*phloroglucinol* (**3b**) *with Ethyl* 4-*Acetoxy*-3-*oxohexanoate* (**2a**).—(2-Methylbutyryl)-phloroglucinol (**3b**) (5.75 g, 27.4 mmol) was taken up in the minimum of cold glacial acetic acid and concentrated sulphuric acid was added dropwise with stirring to produce a 5% v/v sulphuric acid in glacial acetic acid mixture. Ethyl 4-acetoxy-3-oxohexanoate (**2a**) (5.94 g, 27.4 mmol) was added and the mixture left to stand at room temperature. No crystals were

deposited and the mixture was poured onto ice–water after 12 days. The solution was extracted with ether, and the combined extracts were washed with water, dried, and evaporated. The residue was chromatographed on a column of silica gel 50—100 mesh, eluting with chloroform followed by chloroform–methanol (99:1, then 98:2 v/v). Fractions containing starting material (**3b**) were discarded, and the remaining fractions (0.1 g) were separated by h.p.l.c., eluting with hexane–ether (3:1 v/v), to give first 2-*ethyl*-4,6-*dihydroxy*-3-*methyl*-7-(2-*methylbutyryl*)-*benzo*[b]*furan* (**5a**) as yellow needles (17 mg, 0.2%), m.p. 102—104 °C (Found: C, 69.5; H, 7.5%; M^+, 276.1382. $C_{16}H_{20}O_4$ requires C, 69.55; H, 7.3%; *M*, 276.1362); $\nu_{max.}$($CHCl_3$) 3 050 and 1 620 cm^{-1}; $\lambda_{max.}$ 246, 253, 299, and 353 (in base 261 and 356) nm; δ (250 MHz; $CDCl_3$) 1.0 (3 H, t, *J* 7 Hz, *Me*CH_2CH), 1.25 (3 H, d, *J* 7 Hz, *Me*CH), 1.30 (3 H, t, *J* 7 Hz, *Me*CH_2CO), 1.4—1.9 (2 H, m, *J* 7 Hz, MeCH_2CH), 2.75 (2 H, q, *J* 7 Hz, MeCH_2CO), 3.8 (1 H, m, CHCO), 5.85 (1 H, br s, non-chelated OH), 6.15 (1 H, s, ArH), and 13.80 (1 H, s, chelated OH); *m/z* 276 (M^+, 26%), 219 (100), and 191 (2). This was followed by 2-*ethyl*-3-*methoxycarbonylmethyl*-7-(2-*methylbutyryl*)-4,6-*dihydroxy*-*benzo*[b]*furan* (**5b**) as yellow needles (90 mg, 1%), m.p. 117—118 °C (Found: C, 64.7; H, 6.95%; M^+, 334.1466. $C_{18}H_{22}O_6$ requires C, 64.66; H, 6.63%; *M*, 334.1414); $\nu_{max.}$($CHCl_3$) 2 950, 1 700, 1 620, and 1 600 cm^{-1}; $\lambda_{max.}$ 245, 252, 297, and 348 (in base 268 and 353) nm; δ($CDCl_3$) 1.0 (3 H, t, *J* 7 Hz, *Me*CH_2CH), 1.25 (3 H, d, *J* 7 Hz, *Me*CH), 1.36 (3 H, t, *J* 7 Hz, *Me*CH_2CO), 1.4—2.0 (2 H, m, MeCH_2CH), 2.84 (2 H, q, *J* 7 Hz, MeCH_2CO), 3.9 (6 H, m, CH_2CHCO, OMe, and CCH_2CO), 6.48 (1 H, s, ArH), 9.2 (1 H, s, non-chelated OH), and 14.0 (1 H, s, chelated OH); *m/z* 334 (M^+, 60%), 277 (100), and 217 (60). The following reactions were performed in a similiar fashion:

Condensation of (3-*methylbutyryl*)*phloroglucinol* (**3a**) *with ethyl* 4-*acetoxy*-3-*oxohexanoate* (**2a**). This was performed as above using (3-methylbutyryl)phloroglucinol (**3a**) (2.1 g, 10 mmol) and ethyl 4-acetoxy-3-oxohexanoate (**2a**) (2.16 g, 10 mmol). No crystals were deposited and the mixture was poured onto ice–water after 11 days. Work-up as above gave a residue that was chromatographed on a column of silica gel 50—100 mesh, eluting with chloroform followed by chloroform–methanol (200:1 v/v), to afford 3-*carboxymethyl*-2-*ethyl*-4,6-*dihydroxy*-5-(3-*methylbutyryl*)*benzo*[b]*furan* (**5c**) as pale yellow solid (200 mg, 6%), m.p. 210 °C from chloroform–methanol (Found: C, 63.5; H, 6.35%; M^+, 320.1267. $C_{17}H_{20}O_6$ requires C, 63.74; H, 6.29%; *M*, 320.1260); $\nu_{max.}$(KBr) 3 375, 1 720, and 1 620 cm^{-1}; $\lambda_{max.}$ 246, 251, 298, and 348 (in base 261, 267, and 355) nm; δ [90 MHz; $(CD_3)_2CO$] 1.05 (6 H, d, *J* 7 Hz, Me_2CH), 1.35 (3 H, t, *J* 7 Hz, *Me*CH_2CO), 2.3 (1 H, m, Me_2CHCH_2), 2.8 (2 H, q, *J* 7 Hz, MeCH_2CO), 3.05 (2 H, d, *J* 7 Hz, CHCH_2CO), 3.8 (2 H, s, CH_2CO_2H), 6.2 (1 H, s, ArH), 9.0—10.0 (2 H, br s, non-chelated OH and CO_2H), and 13.6 (1 H, s, chelated OH); *m/z* 320 (M^+, 100%), 305 (38), 263 (43), 245 (15), and 217 (58).

Condensation of (2-*methylbutyryl*)*phloroglucinol* (**3b**) *with ethyl* 4-*bromo*-3-*oxohexanoate* (**2b**). This was performed as above using (2-methylbutyryl)phloroglucinol (**3b**) (7.11 g, 34 mmol) and ethyl 4-bromo-3-oxohexanoate (**2b**) (8.03 g, 34 mmol). The mixture was allowed to stand for 20 days and the precipitated solid was removed by filtration, washed with water, and dried (4.0 g, 31%). The filtrate was poured onto ice–water, the mixture was extracted with ether, and the ether extracts were dried and evaporated to give a residue that was shown (t.l.c., ^1H n.m.r.) to contain only unchanged (2-methylbutyryl)-phloroglucinol (**3b**). Crystallisation of the solid from chloroform–methanol gave 5,7-dihydroxy-8-(2-methylbutyryl)-4-propylcoumarin (**12b**) (300 mg) followed by a mixture of 5,7-dihydroxy-8- and 6-(2-methylbutyryl)-4-propylcoumarins, (**12b**) and (**12a**), respectively (0.7 g); both coumarins were identical with authentic samples.[1] The remaining material was chromatographed on silica, eluting with chloroform, to afford 2-*ethyl*-7-*hydroxy*-8-(2-*methylbutyryl*)*furo*[4,3,2-d,e][1]*benzo*-*pyran*-4(2H)-*one* (**11a**) as yellow crystals (1.5 g), m.p. 124—126 °C from hexane–chloroform (Found: C, 67.65; H, 6.25%; M^+, 302.1141. $C_{17}H_{18}O_5$ requires C, 67.54; H, 6.00%; *M*, 302.1154); $\nu_{max.}$ 1 730, 1 650, 1 630, and 1 600 cm^{-1}; $\lambda_{max.}$ 272 and 332 (in base 265 and 392) nm; δ($CDCl_3$) 1.0 (6 H, t, *J* 7 Hz 2 × *Me*CH_2CH), 1.24 (3 H, dd, *J* 7 and 2 Hz, *Me*CH), 1.4—2.3 (4 H, m, 2 × MeCH_2CH), 3.7 (1 H, m, CHCO), 6.0 (2 H, m, OC*H*C=C*H*CO), 6.52 (1 H, s, ArH), and 14.3 (1 H, s, OH); *m/z* 302 (M^+, 100%), 245 (100), and 217 (55).

Condensation of (3-*methylbutyryl*)*phloroglucinol* (**3a**) *with ethyl* 4-*bromo*-3-*oxohexanoate* (**2b**). This was performed as above using (3-methylbutyryl)phloroglucinol (**3a**) (6.3 g, 30 mmol) and ethyl 4-bromo-3-oxohexanoate (**2b**) (7.11 g, 30 mmol). The mixture was allowed to stand for 14 days and the precipitated solid was removed by filtration, washed with water, and dried (4.1 g, 36%). The filtrate was poured onto ice–water, the mixture was extracted with ether, and the ether extracts were dried and evaporated to give a residue that was shown (t.l.c., ^1H n.m.r.) to contain only unchanged (3-methylbutyryl)-phloroglucinol (**3a**). The solid was shown to be a mixture of two components; crystallisation from chloroform–methanol gave a small amount of 4-(1-bromopropyl)-5,7-dihydroxy-6-(3-methylbutyryl)coumarin (**12c**) as a yellow-brown solid, m.p. 205—206 °C (decomp.), that was slightly impure (Found: M^+, 382.0429. $C_{17}H_{19}BrO_5$ requires *M*, 382.0416), $\nu_{max.}$(KBr) 3 250, 2 950, 1 690, and 1 600 cm^{-1}; $\lambda_{max.}$ 280 and 334 (in base 265 and 394) nm; δ[$(CD_3)_2SO$] 0.96, (6 H, d, *J* 7 Hz, Me_2CH), 1.04 (3 H, t, *J* 7 Hz, *Me*CH_2), 1.7—2.3 (3 H, m, Me_2CH and MeCH_2), 2.86 (2 H, t, *J* 6 Hz, CHCH_2CO), 6.02 (1 H, s, C=CHCO), 5.9—6.1 (1 H, m, CHBr), and 6.32 (1 H, s, ArH); the hydroxy protons were not discernible; *m/z* 384 and 382 (M^+, 1%), 302 (65), 287 (44), and 245 (100). The remaining material was chromatographed on silica, eluting with chloroform, to give 2-*ethyl*-7-*hydroxy*-8-(3-*methylbutyryl*)*furo*[4,3,2-d,e][1]*benzo*-*pyran*-4(2H)-*one* (**11b**) as yellow flakes, m.p. 116—118 °C from hexane–chloroform (Found: C, 67.45; H, 6.0%; M^+, 302.1137. $C_{17}H_{18}O_5$ requires C, 67.54; H, 6.00%; *M*, 302.1154); $\nu_{max.}$($CHCl_3$) 1 730, 1 630, and 1 610 cm^{-1}; $\lambda_{max.}$ 271 and 331 (in base 260 and 385) nm; δ($CDCl_3$) 1.04 (6 H, d, *J* 7 Hz, Me_2CH), 1.16 (3 H, t, *J* 7 Hz, *Me*CH_2), 1.9—2.4 (3 H, m, Me_2CH and MeCH_2), 2.86 (2 H, dd, *J* 3 and 7 Hz, CHCH_2CO), 5.62 (1 H, t, *J* 7 Hz, CHO), 5.70 (1 H, d, *J* 2 Hz, CHC=C*H*CO), 6.14 (1 H, s, ArH), and 13.4 (1 H, s, chelated OH); *m/z* 302 (M^+, 83%), 287 (69), 245 (100), and 217 (24).

Reaction of 4-(1-*Bromopropyl*)-5,7-*dihydroxy*-6-(3-*methylbutyryl*)*coumarin* (**12c**) *with Sodium Acetate–Acetic Acid.*—4-(1-Bromopropyl)-5,7-dihydroxy-6-(3-methylbutyryl)coumarin (**12c**) (250 mg, 0.65 mmol) and sodium acetate (0.5 g) were heated at reflux in glacial acetic acid (10 ml) for 24 h. The solvent was then evaporated, the residue partitioned between dilute hydrochloric acid and ether, and the ether layer dried and evaporated. The residue was chromatographed on silica, eluting with chloroform, to give a single product, 2-*ethyl*-4,6-*dihydroxy*-3-*methyl*-7-(3-*methylbutyryl*)*benzo*[b]*furan* (**5d**) as yellow-brown needles (100 mg, 55%), m.p. 185—187 °C from hexane–chloroform (Found: C, 69.35; H, 7.15%; M^+, 276.1374. $C_{16}H_{20}O_4$ requires C, 69.55; H, 7.3%; *M*, 276.1362); $\nu_{max.}$(KBr) 3 200, 2 950, and 1 600 cm^{-1}; $\lambda_{max.}$ 299 and 352 (in base 262 and 356) nm; δ($CDCl_3$) 1.04 (6 H, d, *J* 7 Hz, Me_2CH), 1.28 (3 H, t, *J* 7 Hz, *Me*CH_2), 2.28 (3 H, s, *Me*C=C), 2.3—2.4 (1 H, m, Me_2CH), 2.70 (2 H, q, *J* 7 Hz, MeCH_2), 3.04 (2 H, d, *J* 7 Hz, CH_2CO), 5.85 (1 H, s, non-chelated OH), 6.12 (1 H, s, ArH), and 13.5 (1 H, s, chelated OH); *m/z* 276 (M^+, 100%), 261 (85), and 219 (100).

Condensation of Butyrylphloroglucinol (**3c**) *with Ethyl* 4-*Chloro*-3-*oxobutanoate* (**2d**).—This was performed as usual (see

above) using butyrylphloroglucinol (**3c**) (1.96 g, 10 mmol) and ethyl 4-chloro-3-oxobutanoate (**2d**) (1.65 g, 10 mmol). The mixture was allowed to stand for 7 days and the precipitated solid was removed by filtration, washed with water, and dried (2.4 g, 81%). Crystallisation from chloroform–THF gave 6-*butyryl*-4-*chloromethyl*-5,7-*dihydroxycoumarin* (**12d**) as a yellow solid (1.8 g), m.p. 225—230 °C (decomp.) (Found: 56.8; H, 4.5; Cl, 11.9%; M^+, 296.0442. $C_{14}H_{13}ClO_5$ requires C, 56.67; H, 4.42; Cl, 11.94%; *M*, 296.0451); $\nu_{max.}$(KBr) 1 700 and 1 610 cm^{-1}; $\lambda_{max.}$ 278 and 328 (in base 261 and 351) nm; δ(C_5D_5N) 0.94 (3 H, t, *J* 7 Hz, *Me*CH_2), 1.65 (2 H, m, *J* 7 Hz, *MeCH*$_2$), 2.94 (2 H, t, *J* 7 Hz, CH_2CO), 5.74 (2 H, d, *J* 2 Hz, CH_2Cl), 6.0 (1 H, d, *J* 2 Hz, CH_2C=C*H*CO), 6.36 (1 H, s, ArH), and 15.0 (2 H, br, 2 × OH); *m*/*z* 296 (M^+, 1%), 260 (40), and 217 (100). The remaining material was chromatographed on silica, eluting with chloroform, to give 6-*butyryl*-7-*hydroxyfuro*[4,3,2-d,e][1]-*benzopyran*-4(2H)-*one* (**11c**) as white needles (80 mg), m.p. 150—152 °C from hexane–chloroform (Found: C, 64.6; H, 4.55%; M^+, 260.0695. $C_{14}H_{12}O_5$ requires C, 64.61; H, 4.65%; *M*, 260.0685); $\nu_{max.}$($CHCl_3$) 1 730, 1 660, and 1 620 cm^{-1}; $\lambda_{max.}$ 281 and 325 (in base 270, 348, and 389) nm; δ($CDCl_3$) 1.04 (3 H, t, *J* 7 Hz, *Me*CH_2), 1.76 (2 H, m, *J* 7 Hz, MeC*H*$_2$), 3.16 (2 H, t, *J* 7 Hz, CH_2CO), 5.50 (2 H, d, *J* 2 Hz, OCH_2C), 5.94 (1 H, d, *J* 2 Hz, CH_2C=C*H*CO), 6.08 (1 H, s, ArH), and 14.45 (1 H, s, OH); *m*/*z* 260 (M^+, 40%), 217 (100), and 189 (55). Further elution afforded an impure sample of 8-butyryl-4-chloromethyl-5,7-dihydroxycoumarin (100 mg), m.p. 210—212 °C (decomp.) from chloroform (Found: M^+, 296.0443. $C_{14}H_{13}ClO_5$ requires *M*, 296.0451); $\nu_{max.}$(KBr) 1 690 and 1 620 cm^{-1}; $\lambda_{max.}$ 284 and 319 (in base 348 and 388) nm; δ(C_5D_5N) 1.0 (3 H, t, *J* 7 Hz, *Me*CH_2), 1.75 (2 H, m, *J* 7 Hz, MeC*H*$_2$), 3.24 (2 H, t, *J* 7 Hz, CH_2CO), 5.24 (2 H, br s, CH_2Cl), 5.66 (1 H, d, *J* 2 Hz, CH_2C=C*H*CO), 6.60 (1 H, s, ArH), and 11.10 (2 H, br, 2 × OH); *m*/*z* 296 (M^+, 1%) 260 (40), and 217 (100).

Reaction of 6-*Butyryl*-4-*chloromethyl*-5,7-*dihydroxycoumarin* (**12d**) *with Silver Acetate*.—6-Butyryl-4-chloromethyl-5,7-dihydroxycoumarin (**12d**) (200 mg, 0.67 mmol) and silver acetate were heated at reflux in dry acetonitrile (10 ml) for 24 h. The solvent was evaporated and the residue chromatographed on silica, eluting with chloroform, to give 8-*butyryl*-7-*hydroxyfuro*[4,3,2-d,e][1]*benzopyran*-4(2H)-*one* (**11d**) as white needles (175 mg, 100%), m.p. 153—155 °C from hexane–chloroform (Found: C, 64.55; H, 4.8%; M^+, 260.0669. $C_{14}H_{12}O_5$ requires C, 64.61; H, 4.65%; *M*, 260.0685); $\nu_{max.}$($CHCl_3$) 1 730, 1 650, 1 630, and 1 600 cm^{-1}; $\lambda_{max.}$ 268 and 331 (in base 260 and 350) nm; δ($CDCl_3$) 1.05 (3 H, t, *J* 7 Hz, *Me*CH_2), 1.4—1.9 (2 H, m, MeC*H*$_2$), 3.05 (2 H, t, *J* 7 Hz, CH_2CO), 5.85 (2 H, d, *J* 2 Hz, OCH_2C), 5.9 (1 H, d, *J* 2 Hz, CH_2C=C*H*CO), 6.35 (1 H, s, ArH), and 13.4 (1 H, s, OH); *m*/*z* 260 (M^+, 35%), 217 (100), and 189 (65).

Reaction of 6-*Butyryl*-4-*chloromethyl*-5,7-*dihydroxycoumarin* (**12d**) *with Sodium Acetate–Acetic Acid*.—Coumarin (**12d**) (200 mg, 0.67 mmol) and sodium acetate (0.5 g) were heated at reflux in glacial acetic acid (10 ml) for 24 h. The mixture was poured into water, the solution extracted with ether, and the combined ether extracts were washed with water, dried, and evaporated. The residue was crystallised from hexane–chloroform to give 7-*butyryl*-4,6-*dihydroxy*-3-*methylbenzo*[b]*furan* (**5e**) as yellow-brown needles (100 mg, 59%), m.p. 182—184 °C (Found: C, 66.8; H, 6.3%; M^+, 234.0890. $C_{13}H_{14}O_4$ requires C, 66.66; H, 6.02%; *M*, 234.0892); $\nu_{max.}$(KBr) 3 350 and 1 610 cm^{-1}; $\lambda_{max.}$ 241, 248, 296, and 341 (in base 258 and 350) nm; δ($CDCl_3$–CD_3OD) 1.04 (3 H, t, *J* 7 Hz, *Me*CH_2), 1.4—1.9 (2 H, m, *J* 7 Hz, MeC*H*$_2$CH$_2$), 2.32 (3 H, d, *J* 2 Hz, *Me*C=CH), 3.1 (2 H, t, *J* 7 Hz, CH_2CO), 6.1 (1 H, s, ArH), and 7.2 (1 H, d, *J* 2 Hz, MeC=C*H*); the hydroxy protons were not discernible; *m*/*z* 234 (M^+, 35%), 219 (20), and 191 (100).

Reaction of 6-*Butyryl*-4-*chloromethyl*-5,7-*dihydroxycoumarin* (**12d**) *with Tetramethylammonium Acetate*.—Coumarin (**12d**) (200 mg, 0.67 mmol) and tetramethylammonium acetate[21] (178 mg, 1.34 mmol) were stirred in dry acetone (15 ml) overnight. The solution was evaporated to dryness, the residue taken up in ether, and the ether solution washed with water, dried, and evaporated. Chromatography of the residue on silica, eluting with chloroform, gave 8-*butyryl*-7-*hydroxyfuro*[4,3,2-d,e][1]-*benzopyran*-4(3H)-*one* (**13a**) as yellow needles (147 mg, 84%), m.p. 242—244 °C from methanol–chloroform (Found: C, 64.45; H, 4.7%; M^+, 260.0699. $C_{14}H_{12}O_5$ requires C, 64.61; H, 4.65%; *M*, 260.0685); $\nu_{max.}$($CHCl_3$) 1 790 and 1 640 cm^{-1}; $\lambda_{max.}$ 233, 281, and 345 (in base 261 and 350) nm; δ(C_5D_5N) 0.92 (3 H, t, *J*7 Hz, *Me*CH_2), 1.6—1.9 (2 H, m, MeC*H*$_2$), 2.96 (2 H, t, *J* 7 Hz, CH_2CH_2CO), 4.2 (2 H, s, C=CCH_2CO), 6.8 (1 H, s, ArH), 7.8 (1 H, s, OCH=C), and 13.2 (1 H, s, OH); *m*/*z* 260 (M^+, 100%), 217 (85), and 189 (64).

6-*Butyryl*-5,7-*dimethoxy*-4-*propylcoumarin* (**14b**).—A mixture of 6-butyryl-5,7-dihydroxy-4-propylcoumarin (**14a**)[1] (8.55 g, 29.5 mmol), dimethyl sulphate (2.5 mol equiv.), and anhydrous potassium carbonate (7 mol equiv.) was heated at reflux in dry acetone for 3 h. The cooled solution was filtered, the filtrate evaporated to dryness, and the residue chromatographed on silica, eluting with chloroform, to afford 6-*butyryl*-5,7-*dimethoxy*-4-*propylcoumarin* (**14b**) as white needles (8.6 g, 91%), m.p. 66—68 °C from hexane (Found: C, 68.0; H, 7.05%; M^+, 318.1451. $C_{18}H_{22}O_5$ requires C, 67.91; H, 6.97%; *M*, 318.1467); $\nu_{max.}$(KBr) 1 710 and 1 600 cm^{-1}; $\lambda_{max.}$ 241infl, 250infl, and 332 nm; δ($CDCl_3$) 0.96 and 1.0 (each 3 H, t, *J* 7 Hz, *Me*CH_2), 1.4—1.9 (4 H, m, 2 × MeCH_2CH$_2$), 2.7—2.9 (4 H, m, CH_2CO and CH_2=CHCO), 3.76 and 3.84 (6 H, 2 × s, 2 × MeO), 6.08 (1 H, s, C=CHCO), and 6.64 (1 H, s, ArH); *m*/*z* 318 (M^+, 39%), 275 (100), and 247 (21).

8-*Butyryl*-5,7-*dimethoxy*-4-*propylcoumarin* (**14d**) was prepared as above from 8-butyryl-5,7-dihydroxy-4-propylcoumarin (**14c**)[1] (5.2 g, 17.9 mmol) as white plates (5.4 g, 95%), m.p. 93—95 °C from hexane–chloroform (Found: C, 68.15; H, 7.25%; M^+, 318.1448. $C_{18}H_{22}O_5$ requires C, 67.91; H, 6.97%; *M*, 318.1467); $\nu_{max.}$($CHCl_3$) 1 720 and 1 610 cm^{-1}; $\lambda_{max.}$ 274, 258, and 317 nm; δ($CDCl_3$) 1.0 and 1.04 (each 3 H, t, *J* 7 Hz, *Me*CH_2), 1.4—1.9 (4 H, m, *J* 7 Hz, 2 × MeCH_2CH$_2$), 2.84 and 2.88 (4 H, 2 × t, *J* 7 Hz, CH_2CO and CH_2C=CHCO), 4.00 and 4.04 (6 H, 2 × s, 2 × MeO), 6.04 (1 H, s, C=CHCO), and 6.5 (1 H, s, ArH); *m*/*z* 318 (M^+, 68%), 275 (100), and 247 (65).

4-(1-*Bromopropyl*)-6-*butyryl*-5,7-*dimethoxycoumarin* (**15a**).—6-Butyryl-5,7-dimethoxy-4-propylcoumarin (**14b**) (8.6 g, 30 mmol), freshly recrystallised *N*-bromosuccinimide (1 mol equiv.), and azo(isobutyronitrile) (50 mg) in dry tetrachloromethane (100 ml) were heated at reflux under nitrogen until ^{1}H n.m.r. spectra of the mixture showed complete conversion of coumarin (**14b**) into the bromo derivative. The cooled reaction mixture was filtered and the solid was washed with tetrachloromethane. The filtrates were diluted to 100 ml with chloroform, washed with saturated aqueous sodium hydrogen carbonate, dried, and evaporated to leave a residue that was chromatographed on silica, eluting with chloroform, to give 4-(1-*bromopropyl*)-6-*butyryl*-5,7-*dimethoxycoumarin* (**15a**) as a white solid (10.7 g, 99%), m.p. 91—93 °C from hexane–chloroform (Found: C, 54.6; H, 5.3; Br, 19.75; M^+, 396.0554. $C_{18}H_{21}BrO_5$ requires C, 54.42; H, 5.33; Br, 20.12%; *M*, 396.0573); $\nu_{max.}$($CHCl_3$) 1 720 and 1 600 cm^{-1}; $\lambda_{max.}$ 329 nm; δ($CDCl_3$) 1.0 (3 H, t, *J* 7 Hz, *Me*CH_2CH$_2$), 1.12 (3 H, t, *J* 7 Hz, *Me*CH_2CHBr), 1.5—1.9 (2 H, m, *J* 7 Hz, MeCH_2CH$_2$), 1.95—2.25 (2 H, m, *J* 7 Hz, MeCH_2CHBr), 2.96 (2 H, t, *J* 7 Hz, CH_2CO), 3.84 and 3.86 (6 H, 2 × s, 2 × MeO), 5.8 (1 H, t, *J* 7 Hz, CH_2CHBr), 6.52 (1 H, s, CHBrC=C*H*CO), and 6.64 (1 H, s,

ArH); *m/z* 398 and 396 (M^+, 20%), 355 and 353 (100), 317 (35), 275 (100), and 273 (81).

4-(1-*Bromopropyl*)-8-*butyryl*-5,7-*dimethoxycoumarin* (**15b**) was prepared as above from 8-butyryl-5,7-dimethoxy-4-propylcoumarin (**14d**) (5.3 g, 17 mmol) as a white solid (5.7 g, 86%), m.p. 85—86 °C from hexane–ether (Found: C, 54.75; H, 5.0%; M^+, 396.0573. $C_{18}H_{21}BrO_5$ requires C, 54.42; H, 5.33%; *M*, 396.0573); $\nu_{max.}$($CHCl_3$) 1 720 and 1 610 cm^{-1}; $\lambda_{max.}$ 250 and 326 nm; δ($CDCl_3$) 1.0 (3 H, t, *Me*CH_2CH_2), 1.16 (3 H, t, *J* 7 Hz, *Me*CH_2CHBr), 1.5—1.9 (2 H, m, *J* 7 Hz, $CH_3CH_2CH_2$), 1.9—2.3 (2 H, m, *J* 7 Hz, CH_3CH_2CHBr), 2.84 (2 H, t, *J* 7 Hz, CH_2CO), 4.0 and 4.1 (6 H, 2 × s, 2 × MeO), 6.04 (1 H, t, *J* 7 Hz, CH_2CHBr), 6.56 (1 H, s, CHBrC=C*H*CO), and 6.68 (1 H, s, ArH); *m/z* 398 and 396 (M^+, 8%), 355 and 353 (70), 318 (17), 275 (100), and 273 (80).

4-(1-*Acetoxypropyl*)-6-*butyryl*-5,7-*dimethoxycoumarin* (**16a**).—4-(1-Bromopropyl)-6-butyryl-5,7-dimethoxycoumarin (**15a**) (4.9 g, 12.4 mmol) and tetramethylammonium acetate (2 mol equiv.) were stirred in dry acetone for 2—3 days at 20 °C. The solution was filtered and evaporated to leave a residue that was partitioned between ether and water. The ether layer was washed with water, dried, and evaporated to afford a residue that was chromatographed on silica, eluting with chloroform, to give 4-(1-*acetoxypropyl*)-6-*butyryl*-5,7-*dimethoxycoumarin* (**16a**) as white plates (3.8 g, 82%), m.p. 120—122 °C from hexane–ether (Found: C, 63.85; H, 6.7%; M^+, 376.1540. $C_{20}H_{24}O_7$ requires C, 63.86; H, 6.43%; *M*, 376.1522); $\nu_{max.}$($CHCl_3$) 1 730 and 1 610 cm^{-1}; $\lambda_{max.}$ 243infl, 251infl, and 323 nm; δ($CDCl_3$) 0.98 and 1.0 (each 3 H, t, *J* 7 Hz, *Me*CH_2), 1.5—1.9 (4 H, m, MeCH_2CH_2 and MeCH_2CH), 2.18 (3 H, s, MeCO), 2.76 (2 H, t, *J* 7 Hz, CH_2CO), 3.86 (6 H, s, 2 × MeO), 6.16 (1 H, dd, CHO), 6.24 (1 H, s, C=CHCO), and 6.62 (1 H, s, ArH); *m/z* 376 (M^+, 22%), 334 (20), 333 (100), 291 (40), 273 (12), and 263 (15).

A reaction between bromopropylcoumarin (**15a**) (500 mg, 1.26 mmol) and silver acetate (217 mg, 1.3 mmol) in dry acetonitrile was heated at reflux for 24 h, cooled, filtered through Kieselguhr, and the filtrate evaporated to dryness. Chromatography of the residue on silica, eluting with light petroleum (b.p. 40—60 °C)—chloroform, afforded unchanged coumarin (**15a**) followed by the acetoxypropylcoumarin (**16a**) (190 mg, 40%). A reaction of (**15a**) (300 mg, 0.76 mmol) and sodium acetate (0.5 g) in glacial acetic acid (10 ml) was heated at reflux for 24 h, cooled, and evaporated to dryness. Partition of the residue between ether and dilute hydrochloric acid, followed by drying and evaporating the ether phase, left a residue shown by ^1H n.m.r. spectroscopy to be a 1:1 mixture of starting material (**15a**) and acetoxypropylcoumarin (**16a**).

4-(1-*Acetoxypropyl*)-8-*butyryl*-5,7-*dimethoxycoumarin* (**16e**) was prepared as above from 4-(1-bromopropyl)-8-butyryl-5,7-dimethoxycoumarin (**15b**) (5.5 g, 14 mmol) and tetramethylammonium acetate to give a white solid (4.4 g, 85%), m.p. 130—132 °C from hexane–ether (Found: C, 63.55; H, 6.5%; M^+, 376.1511. $C_{20}H_{24}O_7$ requires C, 63.86; H, 6.43%; *M*, 376.1522); $\nu_{max.}$($CHCl_3$) 1 730, 1 620, and 1 600 cm^{-1}; $\lambda_{max.}$ 246, 258, and 319 nm; δ($CDCl_3$) 1.0 and 1.06 (each 3 H, t, *J* 7 Hz, *Me*CH_2), 1.5—2.0 (4 H, m, MeCH_2CH_2 and MeCH_2CH), 2.22 (3 H, s, MeCO), 2.86 (2 H, t, *J* 7 Hz, CH_2CO), 4.0 and 4.1 (6 H, 2 × s, 2 × MeO), 6.4 (1 H, s, C=CHCO), 6.5 (1 H, m, CHO), and 6.56 (1 H, s, ArH); *m/z* 376 (M^+, 24%), 334 (19), 333 (100), 291 (45), and 273 (23).

Reaction of 4-(1-*Acetoxypropyl*)-6-*butyryl*-5,7-*dimethoxycoumarin* (**16a**) *with Magnesium Iodide*.—4-(1-Acetoxypropyl)-6-butyryl-5,7-dimethoxycoumarin (**16a**) (400 mg, 1 mmol) in dry benzene (40 ml) was treated with magnesium iodide–diethyl ether [5 ml of a solution prepared[22] from magnesium (0.4 g), iodine (2 g), dry ether (2.5 ml) and dry benzene (5 ml) heated to reflux until the solution was colourless] and heated at reflux for 2 h under nitrogen. The cooled solution was acidified with dilute hydrochloric acid and extracted with ether, and the combined ether extracts were washed with water, dried, and evaporated. The residue was chromatographed on silica, eluting with chloroform, to afford 4-(1-*acetoxypropyl*)-6-*butyryl*-5-*hydroxy*-7-*methoxycoumarin* (**16b**) as a yellow solid that crystallised from hexane–chloroform as white needles (345 mg, 90%), m.p. 168—170 °C (Found: C, 63.15; H, 6.45%; M^+, 362.1368. $C_{19}H_{22}O_7$ requires C, 62.98; H, 6.12%; *M*, 362.1365); $\nu_{max.}$($CHCl_3$) 1 730 and 1 600 cm^{-1}; $\lambda_{max.}$ 287 and 322 (in base 233, 284infl, 310, and 394) nm; δ($CDCl_3$) 1.04 (6 H, m, *Me*CH_2CH_2 and *Me*CH_2CH), 1.4—2.0 (4 H, m, MeCH_2CH_2 and MeCH_2CH), 2.18 (3 H, s, MeCO), 3.0 (2 H, t, *J* 7 Hz, CH_2CH_2CO), 3.96 (3 H, s, MeO), 6.18 (1 H, s, CH_2C=C*H*CO), 6.30 (1 H, s, ArH), 6.5 (1 H, dd, CH_2CHOAc), and 15.75 (1 H, s, chelated OH); *m/z* 362 (M^+, 11%), 320 (5), 319 (30), 302 (12), 259 (100), and 231 (17). Further elution with chloroform–methanol (50:1 v/v) afforded 4-(1-*acetoxypropyl*)-6-*butyryl*-5,7-*dihydroxycoumarin* (**17a**) as yellow needles (10 mg, 3%), m.p. 212—214 °C from chloroform–hexane (Found: C, 62.05; H, 5.8%; M^+, 348.1224. $C_{18}H_{20}O_7$ requires C, 61.83; H, 6.08%; *M*, 348.1209); $\nu_{max.}$($CHCl_3$) 1 730, 1 690, and 1 610 cm^{-1}; $\lambda_{max.}$ 281 and 328 (in base 236, 295, and 408) nm; δ (250 MHz; $CDCl_3$) 1.0 and 1.05 (each 3 H, t, *J* 7 Hz, *Me*CH_2), 1.6—1.8 (2 H, m, *J* 7 Hz, MeCH_2CH_2), 1.9—2.1 (2 H, m, *J* 7 and 2 Hz, MeCH_2CH), 2.25 (3 H, s, MeCO), 3.15 (2 H, t, *J* 7 Hz, CH_2CO), 6.15 (1 H, s, CHC=C*H*CO), 6.55 (1 H, dd, *J* 7 and 2 Hz, CH_2CHOAc), 6.6 (1 H, s, ArH), 7.05 (1 H, s, non-chelated OH), and 15.85 (1 H, s, chelated OH); *m/z* 348 (M^+, 1%), 288 (53), 245 (100), and 217 (18). When the reaction was repeated with extended reflux (24 h), work-up as above and chromatography on silica, eluting with light petroleum (b.p. 40—60 °C)–chloroform, gave 8-*butyryl*-2-*ethyl*-7-*hydroxyfuro*[4,3,2-d,e][1]*benzopyran*-4(2H)-*one* (**11e**) as yellow needles (222 mg, 73%), m.p. 163—166 °C from hexane–chloroform (Found: C, 66.6; H, 5.9%; M^+, 288.0973. $C_{16}H_{16}O_5$ requires C, 66.66; H, 5.59%; *M*, 288.0998); $\nu_{max.}$($CHCl_3$), 1 730, 1 630, and 1 600 cm^{-1}; $\lambda_{max.}$ 270 and 331 (in base 265 and 358) nm; δ($CDCl_3$) 1.02 and 1.12 (each 3 H, t, *J* 7 Hz, *Me*CH_2), 1.4—1.9 (2 H, m, *J* 7 Hz, MeCH_2CH_2), 1.9—2.2 (2 H, m, MeCH_2CH), 2.96 (2 H, t, *J* 7 Hz, CH_2CH_2CO), 5.72 (1 H, t, *J* 7 Hz, CH_2CHO), 5.8 (1 H, s, CHC=C*H*CO), 6.26 (1 H, s, ArH), and 13.4 (1 H, s, chelated OH); *m/z* 288 (M^+, 45%), 245 (100), and 217 (20). This was followed by the monohydroxycoumarin (**16b**) (25 mg, 6%).

Reaction of 4-(1-*Acetoxypropyl*)-6-*butyryl*-5,7-*dimethoxycoumarin* (**16a**) *with Boron Tribromide*.—To 4-(1-acetoxypropyl)-6-butyryl-5,7-dimethoxycoumarin (**16a**) (0.4 g, 1 mmol) in dry dichloromethane (20 ml) at −78 °C under nitrogen was added boron tribromide (0.5 ml) with stirring. The solution was kept at −78 °C for 2 h then allowed to warm to 0 °C when it was poured into a dilute hydrochloric acid–ice mixture. The mixture was extracted with chloroform and the organic phase dried and evaporated. The residue was chromatographed on silica, eluting with hexane–chloroform (1:1 v/v), to give first 4-(1-acetoxypropyl)-6-butyryl-5-hydroxy-7-methoxycoumarin (**16b**) (81 mg, 21%), m.p. 168—170 °C, identical with a sample prepared earlier (see above). This was followed by a mixture (100 mg, 26%) of 5-hydroxy-7-methoxycoumarin (**16b**) and the 7-hydroxy-5-methoxycoumarin (**16c**), and finally pure 4-(1-*acetoxypropyl*)-6-*butyryl*-7-*hydroxy*-5-*methoxycoumarin* (**16c**) as white needles (162 mg, 42%), m.p. 129—131 °C from hexane (Found: C, 63.15; H, 6.4%; M^+, 362.1388. $C_{19}H_{22}O_7$ requires C, 62.98; H, 6.12%; *M*, 362.1366); $\nu_{max.}$($CHCl_3$) 1 730, 1 640, and 1 610 cm^{-1}; $\lambda_{max.}$ 258 and 326 (in base 235 and 385) nm; δ($CDCl_3$) 0.98 and 1.06 (each 3 H, t, *J* 7 Hz, *Me*CH_2),

1.5—2.1 (4 H, m, $MeCH_2CH_2$ and $MeCH_2CH$), 2.22 (3 H, s, MeCO), 2.9—3.3 (2 H, m, CH_2CO), 3.96 (3 H, s, MeO), 6.2—6.4 (2 H, m, OCHC=CHCO), 6.64 (1 H, s, ArH), and 12.2 (1 H, s, ArH); *m/z* 362 (M^+, 50%), 319 (100), 302 (10), 277 (70), 259 (90), and 249 (20).

When this reaction was repeated with boron trichloride in place of boron tribromide, a 1:1 mixture of monohydroxycoumarin isomers (**16b** and **c**) was isolated in 90% combined yield. In a further experiment the dimethoxycoumarin (**16a**) (188 mg, 0.5 mmol) was added at 0 °C to a stirred solution of ethanethiol (2 ml) in dry dichloromethane (2 ml) containing aluminium trichloride (0.33 g, 2.5 mmol). Stirring at 0 °C was continued for 1 h, and the mixture then poured into water. Dilute hydrochloric acid (5 ml) was added, the solution extracted with chloroform, and the combined organic extracts were dried and evaporated to leave a residue shown by ^1H n.m.r. spectroscopy and t.l.c. to be a mixture of the monohydroxycoumarin isomers (**16b** and **c**).

4-(1-*Acetoxypropyl*)-6-*butyryl*-5,7-*dihydroxycoumarin* (**17a**).—To a mixture of 4-(1-acetoxypropyl)-6-butyryl-5-hydroxy-7-methoxycoumarin (**16b**) and the 7-hydroxy-5-methoxy isomer (**16c**) (see above) (280 mg, 0.77 mmol) and triethylamine (1 ml) in dry dichloromethane (20 ml) at 0 °C under nitrogen was added trimethylsilyl chloride (1 ml). The mixture was stirred for 30 min and the solvents were then evaporated under reduced presssure. The residue was taken up in dry dichloromethane (20 ml) and the solution cooled to −78 °C under nitrogen. Boron tribromide (0.5 ml) was added and the mixture stirred and allowed to warm to 0 °C. After stirring for 1 h the mixture was poured into dilute hydrochloric acid–ice and extracted with chloroform followed by ether. The combined organic extracts were dried and evaporated to leave a residue that was chromatographed on silica, eluting with chloroform, to give first unchanged coumarins (**16b** and **c**) (180 mg, 64%). Further elution with chloroform–methanol (50:1 v/v) afforded 4-(1-acetoxypropyl)-6-butyryl-5,7-dihydroxycoumarin (**17a**) (78 mg, 29%), m.p. 212—214 °C, identical with a sample prepared earlier (see above).

5-*Acetoxy*-4-(1-*acetoxypropyl*)-6-*butyryl*-7-*methoxycoumarin* (**16d**).—4-(1-acetoxypropyl)-6-butyryl-5-hydroxy-7-methoxycoumarin (**16b**) (0.5 g, 1.4 mmol) was treated with acetic anhydride (5 ml) in dry pyridine (25 ml) for 2 days. The mixture was then poured onto ice–water, acidified with dilute hydrochloric acid, and extracted with ether. The combined organic extracts were washed with water, dried, and evaporated. Crystallisation of the residue from hexane–ether gave 5-*acetoxy*-4-(1-*acetoxypropyl*)-6-*butyryl*-7-*methoxycoumarin* (**16d**) as white needles (400 mg, 72%), m.p. 132—134 °C (Found: C, 62.35; H, 6.25%; M^+, 404.1480. $C_{12}H_{24}O_8$ requires C, 62.37; H, 5.98%; *M*, 404.1472); $\nu_{max.}$($CHCl_3$) 1 780, 1 730, and 1 610 cm^{-1}; $\lambda_{max.}$ 249 and 324 nm; δ (90 MHz; $CDCl_3$) 0.95 (6 H, t, *J* 7 Hz, 2 × $MeCH_2$), 1.4—2.0 (4 H, m, $MeCH_2CH_2$ and $MeCH_2CH$), 2.15 and 2.4 (6 H, 2 × s, 2 × CH_3CO), 2.8 (2 H, t, *J* 7 Hz, CH_2CO), 3.95 (3 H, s, MeO), 6.25 (1 H, dd, *J* 7 and 2 Hz, CH_2CHOAc), 6.45 (1 H, s, CHC=C*H*CO), and 6.85 (1 H, s, ArH); *m/z* 404 (M^+, 8%), 361 (45), 319 (100), and 259 (100).

6-*Butyryl*-5,7-*dihydroxy*-4-(1-*hydroxypropyl*)*coumarin* (**12e**).—To 5-acetoxy-4-(1-acetoxypropyl)-6-butyryl-7-methoxycoumarin (**16d**) (150 mg, 0.4 mmol) in dry dichloromethane (20 ml) at −78 °C under nitrogen was added boron tribromide (0.5 ml). The mixture was stirred at −78 °C for 2 h then poured into ice–water, extracted with ether followed by chloroform, and the combined organic extracts were dried and evaporated. The residue was chromatographed on silica, eluting first with chloroform to afford starting coumarin (**16d**) (40 mg, 27%), and then with chloroform–methanol (50:1 v/v) to give 6-*butyryl*-5,7-*dihydroxy*-4-(1-*hydroxypropyl*)*coumarin* (**12e**) as yellow needles (80 mg, 70%), m.p. 226—228 °C from chloroform–methanol (Found: C, 62.75; H, 6.1%; M^+, 306.1100. $C_{16}H_{18}O_6$ requires C, 62.74; H, 5.92%; *M*, 306.1103); $\nu_{max.}$($CHCl_3$) 3 450, 1 700, and 1 610 cm^{-1}; $\lambda_{max.}$ 281 and 323 (in base 293 and 402) nm; δ (90 MHz; C_5D_5N) 1.0 and 1.3 (each 3 H, t, *J* 7 Hz, $MeCH_2$), 1.5—2.4 (4 H, m, $MeCH_2CH_2$ and $MeCH_2CH$), 3.35 (2 H, t, *J* 7 Hz, CH_2CO), 5.9 (1 H, m, CH_2CHOH), 6.5 (1 H, s, ArH), 7.15 (1 H, s, CHC=C*H*CO, and 11.85 (3 H, br s, 3 × OH); *m/z* 306 (M^+, 55%), 288 (8), 263 (11), 249 (45), 245 (100), and 217 (16).

Reaction of 4-(1-*Acetoxypropyl*)-6-*butyryl*-5,7-*dihydroxycoumarin* (**17a**) *with Aqueous Potassium Hydroxide*.—4-(1-Acetoxypropyl)-6-butyryl-5,7-dihydroxycoumarin (**17a**) (10 mg) was treated with 10% aqueous potassium hydroxide (1 ml) at 0 °C for 1.5 h. The solution was acidified with dilute hydrochloric acid and extracted with ether. T.l.c. examination of the dried ether extracts showed no starting material to be present but complete conversion to 6-butyryl-5,7-dihydroxy-4-(1-hydroxypropyl)coumarin (**12e**) (see above). When the procedure was repeated with 5% aqueous potassium hydroxide (2 equiv.), t.l.c. examination of the extracts showed the presence of starting material (**17a**) with only a trace of hydrolysis product (**12e**).

Mammea E/AC (**17b**).—4-(1-Acetoxypropyl)-6-butyryl-5,7-dihydroxycoumarin (**17a**) (0.5 g, 1.44 mmol) in 5% aqueous potassium hydroxide (3 ml, 2.88 mmol) was stirred at 0 °C under nitrogen during the addition of 3-methylbut-2-enyl bromide (0.22 g, 1.47 mmol) over 1.5 h. The solution was acidified with dilute hydrochloric acid, extracted with ether followed by chloroform, and the combined organic extracts were dried and evaporated. Chromatography of the residue on silica, eluting with hexane–chloroform (1:4 v/v), gave some gum followed by *mammea E/AC* (**17b**) as yellow needles (125 mg, 21%), m.p. 139—141 °C from hexane–chloroform (Found: C, 66.05; H, 6.95%; M^+, 416.1832. $C_{23}H_{28}O_7$ requires C, 66.33; H, 6.78%; *M*, 416.1835); $\nu_{max.}$($CHCl_3$) 1 730 and 1 620 cm^{-1}; $\lambda_{max.}$ 237, 283, and 308infl (in base 238, 297, and 415) nm; δ($CDCl_3$) 1.0 (6 H, m, 2 × $MeCH_2$), 1.2—2.0 (4 H, m, $MeCH_2CH_2$ and $MeCH_2CH$), 1.68 and 1.76 (6 H, 2 × s, Me_2C=CH), 2.28 (3 H, s, MeCO), 3.22 (2 H, t, *J* 7 Hz, CH_2CO), 3.68 (2 H, d, *J* 7 Hz, C=CHCH_2), 5.36 (1 H, t, C=C*H*CH_2), 6.4 (1 H, s, C=CHCO), 6.76 (1 H, dd, *J* 2 and 7 Hz, OC*H*C=CH), 7.48 (1 H, s, non-chelated OH), and 15.75 (1 H, s, chelated OH); *m/z* 416 (M^+, 4%), 356 (69), 341 (100), 313 (45), and 301 (80). Continued elution with chloroform followed by chloroform–methanol (50:1 v/v) gave unchanged starting material (**17a**) (125 mg, 25%) and then the trihydroxycoumarin (**12e**) (15 mg, 2%), identical with a sample prepared earlier (see above).

4-(1-*Acetoxypropyl*)-8-*butyryl*-7-*hydroxy*-5-*methoxycoumarin* (**16f**).—To 4-(1-acetoxypropyl)-8-butyryl-5,7-dimethoxycoumarin (**16e**) (3.9 g, 10.4 mmol) in dry dichloromethane (100 ml) at −78 °C under nitrogen was added boron tribromide (3 ml). The mixture was allowed to warm to 0 °C with stirring, and then poured into dilute hydrochloric acid–ice and extracted with chloroform and ether. The combined organic extracts were dried and evaporated to leave a residue that was chromatographed on a silica column, eluting with chloroform, to afford 4-(1-*acetoxypropyl*)-8-*butyryl*-7-*hydroxy*-5-*methoxycoumarin* (**16f**) as white needles (3.3 g, 88%), m.p. 136—138 °C from hexane–chloroform (Found: C, 62.7; H, 6.35%; M^+, 362.1369. $C_{19}H_{22}O_7$ requires C, 62.98; H, 6.12%; *M*, 362.1365), $\nu_{max.}$($CHCl_3$) 1 740 and 1 630 cm^{-1}; $\lambda_{max.}$ 287 and 321 (in base 294 and 383) nm; δ($CDCl_3$) 1.08 (6 H, t, *J* 7 Hz, 2 × $MeCH_2$),

1.6—2.1 (4 H, m, $MeCH_2CH_2$ and $MeCH_2CH$), 2.28 (3 H, s, MeCO), 3.38 (2 H, t, *J* 7 Hz, CH_2CO), 4.14 (3 H, s, MeO), 6.5—6.7 (3 H, m, OCHC=CHCO and ArH), and 14.4 (1 H, s, chelated OH); *m/z* 362 (M^+, 55%), 320 (19), 319 (90), 277 (100), 259 (95), and 231 (25).

8-*Butyryl*-5,7-*dihydroxy*-4-(1-*hydroxypropyl*)*coumarin* (**12f**).—To a solution of 4-(1-acetoxypropyl)-8-butyryl-7-hydroxy-5-methoxycoumarin (**16f**) (230 mg, 0.6 mmol) in HMPA (1 ml) was added lithium t-butyl sulphide in HMPA [15 ml of a solution prepared[23] from t-butyl thiol (2.3 ml) and lithium hydride (1 g) in dry HMPA heated to 50 °C for 2 h] and the mixture was heated at 75 °C for 2 h under nitrogen. The cooled solution was poured into aqueous ammonium chloride, acidified with dilute hydrochloric acid, and extracted with ether. The combined extracts were washed with water, dried, and evaporated to leave a residue that was chromatographed on a silica column to afford 8-*butyryl*-5,7-*dihydroxy*-4-(1-*hydroxypropyl*)*coumarin* (**12f**) as a white solid (50 mg, 26%), m.p. 180—183 °C from chloroform–methanol (Found: C, 62.75; H, 6.25%; M^+, 306.1091. $C_{16}H_{18}O_6$ requires C, 62.74; H, 5.92%; *M*, 306.1103); $\nu_{max.}$($CHCl_3$) 1 730 and 1 630 cm^{-1}; $\lambda_{max.}$ 289 and 317 (in base 244, 345, and 388) nm; δ [90 MHz; $(CD_3)_2CO$] 1.0 and 1.05 (each 3 H, t, *J* 7 Hz, $MeCH_2$), 1.3—2.0 (4 H, m, $MeCH_2CH_2$ and $MeCH_2CH$), 3.20 (2 H, d, *J* 7 Hz, CH_2CH_2CO), 5.3 (1 H, dd, *J* 4 and 7 Hz, CH_2CHOH), 6.3 (1 H, s, ArH), 6.5 (1 H, s, CHC=CHCO), and 13.9 (1 H, s, chelated OH); the non-chelated hydroxy protons were not discernible; *m/z* 306 (M^+, 55%), 263 (100), 245 (100), and 217 (20).

5,7-*Diacetoxy*-4-(1-*acetoxypropyl*)*coumarin* (**16g**).—Acetic anhydride (10 ml) was added to 5,7-dihydroxy-4-(1-hydroxypropyl)coumarin (1.3 g, 5.5 mmol) in dry pyridine (10 ml). After 2 days at 20 °C the solution was poured into ice–water containing dilute hydrochloric acid. The mixture was extracted with chloroform and the organic layer was washed with further portions of dilute hydrochloric acid, dried, and evaporated. Crystallisation of the residue from chloroform–hexane gave 5,7-*diacetoxy*-4-(1-*acetoxypropyl*)*coumarin* (**16g**) as white crystals (1.7 g, 85%), m.p. 116—118 °C (Found: C, 59.7; H, 5.1%; M^+, 362.1008. $C_{18}H_{18}O_8$ requires C, 59.69; H, 5.01%; *M*, 362.1002); $\nu_{max.}$($CHCl_3$) 1 790, 1 780, 1 740, and 1 620 cm^{-1}; $\lambda_{max.}$ 243infl, 286, and 310infl nm; δ ($CDCl_3$) 1.0 (3 H, t, *J* 7 Hz, $MeCH_2$), 1.5—2.1 (2 H, m, $MeCH_2CH$), 2.20, 2.32, and 2.46 (9 H, 3 × s, 3 × MeCO), 6.44 (1 H, dd, *J* 4 and 8 Hz, CH_2CHO), 6.56 (1 H, s, CHC=CHCO), 7.02 and 7.12 (each 1 H, d, ArH); *m/z* 362 (M^+, 5%), 320 (25), 278 (48), 218 (100), 203 (38), and 190 (22).

Selective Deacylation of 5,7-*Diacetoxy*-4-(1-*acetoxypropyl*)*coumarin* (**16g**).—Activated zinc[16] was added to a stirred solution of 5,7-diacetoxy-4-(1-acetoxypropyl)coumarin (**16g**) (1.6 g, 4.4 mmol) in dry methanol. After stirring at 20 °C overnight the solution was filtered on Kieselguhr and the filtrate evaporated to leave 4-(1-acetoxypropyl)-5,7-dihydroxycoumarin (**16h**) (1.2 g, 98%) identical with an authentic sample.[8]

5,7-*Diacetoxy*-6-*butyryl*-4-*propylcoumarin* (**14e**).—Acetic anhydride (20 ml) was added to 6-butyryl-5,7-dihydroxy-4-propylcoumarin (**14a**) (3 g, 10.3 mmol) in dry pyridine (100 ml). After 2 days at 20 °C the reaction was worked up as for (**16g**) above to leave a residue that was crystallised from ethanol to give 5,7-*diacetoxy*-6-*butyryl*-4-*propylcoumarin* (**14e**) as white needles (2.73 g, 71%), m.p. 125—127 °C (Found: C, 64.25; H, 6.2%; M^+, 374.1343. $C_{20}H_{22}O_7$ requires C, 64.14; H, 5.92%; *M*, 374.1365); $\nu_{max.}$($CHCl_3$) 1 780, 1 730, and 1 620 cm^{-1}; $\lambda_{max.}$ 244, 280, and 310 nm; δ($CDCl_3$) 1.0 and 1.05 (each 3 H, t, *J* 7 Hz, $MeCH_2$), 1.4—1.9 (4 H, m, 2 × $MeCH_2$), 2.35 (6 H, s, 2 × MeCO), 2.8 (4 H, m, CH_2CO and CH_2C=CHCO), 6.3 (1 H, s, C=CHCO), and 7.25 (1 H, s, ArH); *m/z* 374 (M^+, 15%), 332 (50), 290 (100), and 247 (89).

5,7-*Diacetoxy*-4-(1-*bromopropyl*)-6-*butyrylcoumarin* (**15c**).—5,7-Diacetoxy-6-butyryl-4-propylcoumarin (**14e**) (2.3, 6.15 mmol) and freshly recrystallised *N*-bromosuccinimide (1.10 g, 6.18 mmol) were suspended in dry tetrachloromethane (60 ml). A trace of azo(isobutyronitrile) was added and the mixture heated at reflux under nitrogen for 2 days, when ^1H n.m.r. spectra of the mixture showed complete disappearance of starting material. The cooled mixture was filtered, diluted to 100 ml with chloroform, and washed with saturated aqueous sodium hydrogen carbonate. The organic layer was dried and evaporated, and the residue was chromatographed on silica, eluting with chloroform, to give 5,7-*diacetoxy*-4-(1-*bromopropyl*)-6-*butyrylcoumarin* (**15c**) (1.7 g, 61%), m.p. 84—85 °C (from hexane–chloroform) (Found: C, 53.1; H, 4.9; Br, 18.3%; M^+, 452.0473. $C_{20}H_{21}BrO_7$ requires C, 52.98; H, 4.64; Br, 17.66%; *M*, 452.0471); $\nu_{max.}$($CHCl_3$) 1 780, 1 740, 1 700, 1 620, and 1 600 cm^{-1}; $\lambda_{max.}$ 241, 295, and 313 nm; δ (90 MHz; $CDCl_3$) 1.0 and 1.15 (each 3 H, t, *J* 7 Hz, $MeCH_2$), 1.45—1.85 (2 H, m, $MeCH_2CH_2$), 2.05—2.35 (2 H, m, $MeCH_2CHBr$), 2.35 and 2.37 (6 H, 2 × s, 2 × MeCO), 2.8 (2 H, t, *J* 7 Hz, CH_2CO), 5.5 (1 H, t, *J* 7 Hz, CHBr), 6.73 (1 H, s, C=CHCO), and 7.3 (1 H, s, ArH); *m/z* 454 and 452 (M^+, 4%) 412 and 410 (22), 370 and 368 (95), 331 (55), 327 and 325 (24), 289 (100), and 288 (90).

Reaction of 5,7-*Diacetoxy*-4-(1-*bromopropyl*)-6-*butyrylcoumarin* (**15c**) *with Tetramethylammonium Acetate*.—5,7-Diacetoxy-4-(1-bromopropyl)-6-butyrylcoumarin (**15c**) (1.55 g, 3.42 mmol) and tetramethylammonium acetate (0.91 g, 6.85 mmol) were stirred in dry acetone (15 ml) for 1 h. The solution was evaporated to dryness, partitioned between water and ether, and the ether layer was washed with water, dried, and evaporated to leave a white solid (0.65 g, 98%), m.p. 234—236 °C from hexane–chloroform, identified as 7-*acetoxy*-8-*butyryl*-2-*ethylfuro*[4,3,2-d,e][1]*benzopyran*-4(3H)-*one* (**13b**) (Found: C, 65.55; H, 5.5%; M^+, 330.1117. $C_{18}H_{18}O_6$ requires C, 65.45; H, 5.49%; *M*, 330.1103); $\nu_{max.}$($CHCl_3$) 1 780, 1 690, and 1 610 cm^{-1}; $\lambda_{max.}$ 234, 274, and 299 nm; δ($CDCl_3$) 1.0 and 1.36 (each 3 H, t, *J* 7 Hz, $MeCH_2$), 1.6—2.0 (2 H, m, *J* 7 Hz, $MeCH_2CH_2$), 2.35 (3 H, s, MeCO), 2.8—3.0 (2 H, q, *J* 7 Hz, $MeCH_2C$=C), 3.12 (2 H, t, *J* 7 Hz, CH_2O), 4.04 (2 H, br s, C=CCH_2CO), and 7.4 (1 H, s, ArH); *m/z* 330 (M^+, 10%), 288 (100), 245 (73), and 217 (60).

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