Synthesis of the *Calophyllum* coumarins. Part 2[1]

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Synthetic routes leading to the synthesis of the natural 4-phenyl, 4-propyl and 4-methyl coumarins isolated from *Calophyllum sp.* are presented. 4-Aryl or -alkyl, 8- and 6-acyl 5,7-dihydroxy coumarins were chromenylated and then methylated at the 5 or 7 positions. A 4-step hydrobromination–bromination–double dehydrobromination sequence converted the 2-methylbutanoyl side chain into the (*E*)-2-methylbut-2-enoyl (tigloyl) group to give calophyllolide, oblongulide, their natural 4-propyl analogue and the corresponding regioisomers. Demethylation and cyclisation of the tigloyl group gave inophyllums C and E, tomentolides A and B, and calanolide D. Sodium boranuide reduction of the 2,3-dimethylchromanone ring afforded inophyllums A, B, D and P, soulattrolide, calanolides A-C, costatolide, and cordatolides A and B. The structures of calanolides C and D, oblongulide and apetatolide have been reassigned. The previously unknown stereochemistry about the 2,3-dimethylchromanone ring of tomentolides A and B has been established as *trans*.

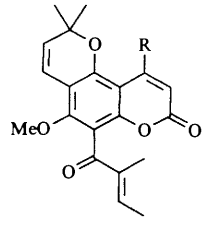
Introduction

Extraction of several tropical plants of the genus *Calophyllum* (Guttiferae) has over the last 35 years led to the isolation of over 20 pyranocoumarins sharing a common 4-alkyl or aryl-5,7-dioxygenated coumarin (coumarin = 2*H*-chromen-2-one) skeleton. Densely functionalised, they can be structurally subdivided into 3 series based upon the nature of a common 2-methylbut-2-enoyl group, or its modification, attached to the aromatic ring.

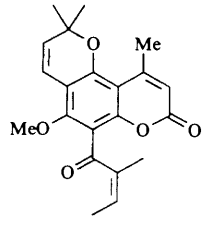
Series A, contains those pyranocoumarins with an uncyclised (*E*)- or (*Z*)-2-methylbut-2-enoyl group, and includes calophyllolide **1** isolated from *C. inophyllum*[2] and *C. bracteatum*,[3] an unnamed propyl analogue **2** from *C. inophyllum*,[4] and oblongulide **3** from *C. cordato-oblongum*.[5] Apetatolide **4** isolated from *C. apetalum*,[6] is a regioisomer of calophyllolide **1**. Ponnalide **5** with a saturated 2-methylbutanoyl group, isolated from *C. inophyllum*,[7,8] can also be added to this series based on close structural similarity to calophyllolide **1**. Calanone **6** recently isolated from *C. teysmannii*,[9] is related to ponnalide but contains a benzoyl group in place of the 2-methylbutanoyl side chain at the 8-position of the coumarin nucleus.

Series B contains those pyranocoumarins which possess a 2,3-dimethylchromanone ring which represents cyclisation of the 2-methylbut-2-enoyl group with the *ortho* oxygen. Inophyllum C (also known as inophyllolide) **7** and inophyllum E **8**, both isolated from *C. inophyllum*,[2,10] are *trans* and *cis* isomers about C-10 and C-11. Calanolide D **9**, the propyl analogue of inophyllum E, has recently been isolated from *C. lanigerum*.[11] Tomentolide A **10** and tomentolide B **11**, isolated from *C. tomentosum*,[6] are regioisomers of inophyllums C **7** and E **8**, and calanolide D **9**, respectively, but their stereochemistry about C-6 and C-7 has not yet been established. Calaustralin **12**, isolated from *C. australianum*,[12] and *C. inophyllum*,[13] unlike other *Calophyllum* coumarins possesses a linear fused ring system and contains an uncyclised 3-methylbut-2-enyl (prenyl) group rather than the more usual 2,2-dimethylchromene ring.

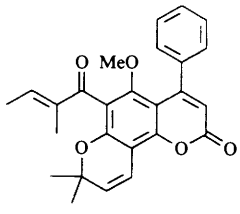
Series C, the largest group, contains those pyranocoumarins in which the 2-methylbut-2-enoyl moiety may be regarded as having undergone cyclisation and reduction to form a 2,3-dimethylchromanol ring. Inophyllum B **13** isolated from *C. inophyllum*,[10] calanolide A **14** from *C. lanigerum*,[11] and



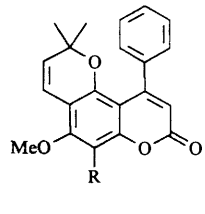
calophyllolide **1** R = Ph
2 R = Pr



oblongulide **3**



apetatolide **4**



ponnalide **5** R = COCHMeEt
calanone **6** R = COPh

cordatolide A **17** from *C. cordato-oblongum*,[5] are reported to all possess a 12β-hydroxy-10β,11α-dimethyl substitution pattern about the chromane ring. Inophyllum P **18** isolated from *C. inophyllum*,[14] calanolide B **19** from *C. lanigerum*,[11] together with cordatolide B **21** from *C. cordato-oblongum*,[5] are reported to all possess the 12α-hydroxy-10β,11α-dimethyl substitution pattern. Soulattrolide **22** isolated from *C. soulattri*,[15] *C. moonii*,[16] and *C. teysmannii*,[17] and costatolide **23** from *C. costatum*,[18] and *C. teysmannii*,[17] are enantiomers of inophyllum P **18** and calanolide B **19**, respectively. In addition, the derivatives 12-acetoxycalanolide A **15**, 12-methoxycalanolide A **16** and 12-methoxycalanolide B **20** have been isolated from *C. lanigerum*.[11] Inophyllum A **24**, isolated from *C. inophyllum*,[10] and *C. moonii*,[16] and calanolide C **25**, isolated from *C. lanigerum*,[11] both have a 12β-hydroxy-10β,11β-dimethyl substitution pattern about the chromane ring and are therefore the C-11 epimers of inophyllum B **13** and calanolide A **14**, respectively. Inophyllum D **26**, isolated from *C. inophyllum*,[10] with the 12α-hydroxy-10β,11β-dimethyl substitution pattern, is

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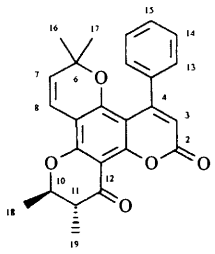
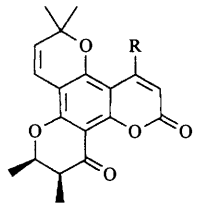
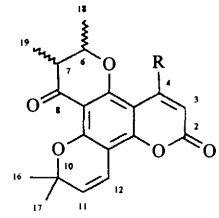


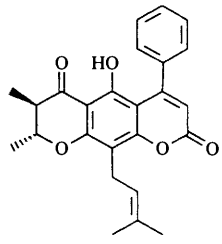
inophyllum C 7



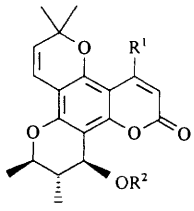
inophyllum E **8** R = Ph
calanolide D **9** R = Pr



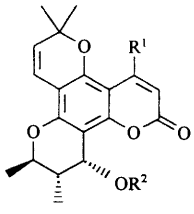
tomentolide A **10** R = Ph
tomentolide B **11** R = Pr



calaustralin **12**



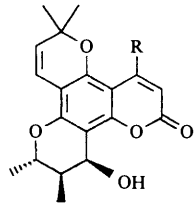
inophyllum B **13** R^1 = Ph, R^2 = H
calanolide A **14** R^1 = Pr, R^2 = H
12-acetoxycalanolide A **15** R^1 = Pr, R^2 = Ac
12-methoxycalanolide B **16** R^1 = Pr, R^2 = Me
cordatolide A **17** R^1 = Me, R^2 = H



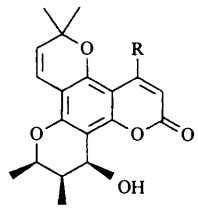
inophyllum P **18** R^1 = Ph, R^2 = H
calanolide B **19** R^1 = Pr, R^2 = H
12-methoxycalanolide B **20** R^1 = Pr, R^2 = Me
cordatolide B **21** R^1 = Me, R^2 = H

the C-11 epimer of inophyllum P **18**. Finally, inophyllums G-1 **27** and G-2 **28**, each with a fused dimethylcyclopropyldihydrofuran ring, have been isolated from *C. inophyllum*.[14] Interestingly, inophyllums A–E and calophyllolide have also been isolated from the giant African snail *Achatina fulica*, which is known to feed on the leaves of *C. inophyllum*.[14]

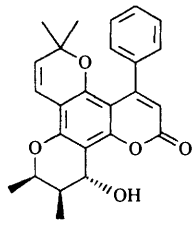
Recent interest in the *Calophyllum* coumarins has arisen as a result of their identification as potent inhibitors of human immunodeficiency virus-1 reverse transcriptase (HIV-1 RT). In



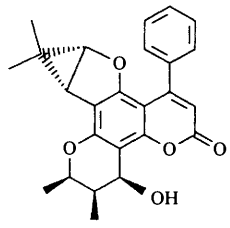
soulattrolide **22** R = Ph
costatolide **23** R = Pr



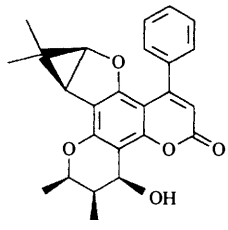
inophyllum A **24** R = Ph
calanolide C **25** R = Pr



inophyllum D **26**



inophyllum G-1 **27**



inophyllum G-2 **28**

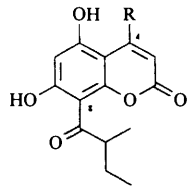
particular, calanolides A **14** and B **19**, inophyllums B **13** and P **18**, soulattrolide **22** and costatolide **23** are reported to be highly active in inhibiting HIV-1 replication and cytopathicity and are active against resistant variant strains of HIV-1.[11,14,17,19–21] Calophyllolide **1** has been reported to exhibit high oral anticoagulant,[22] anti-tubercular,[23] anti-inflammatory[24,25] and anti-arthritic[25] activities. Inophyllums A–E **24**, **13**, **7**, **26** and **8** also exhibit piscicidal activity.[10]

This mix of biological activities, together with the sparse supply of the active natural materials, has led us to embark on a programme of total synthesis in order to make them readily available.‡

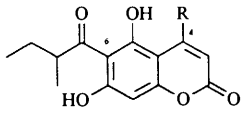
Results and discussion

In our approach, we sought a general synthetic route that would provide access to both regioisomer series, suitable for preparing both the natural materials and their non-natural analogues for structure–activity studies. Previous work by one of us had shown that good yields of 6- and 8-acyl-4-alkyl-5,7-dihydroxy coumarins could be prepared from Pechmann condensation of an acyl phloroglucinol with a β-keto ester using glacial acetic acid containing 5% sulfuric acid as condensing agent.[26] Accordingly, we used this method to prepare acylated coumarins in the 4-methyl and 4-propyl series **30**, **31**, **33** and **34**, obtaining yields of 70–80% with an 6-acyl to 8-acyl isomer ratio of generally *ca.* 3:2. However, this route provided only modest

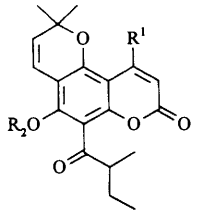
‡ All synthetic compounds with asymmetric centres in this study have been synthesised as the (±) form.



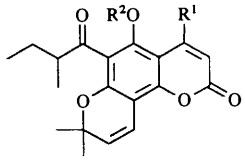
29 R = Ph
30 R = Pr
31 R = Me



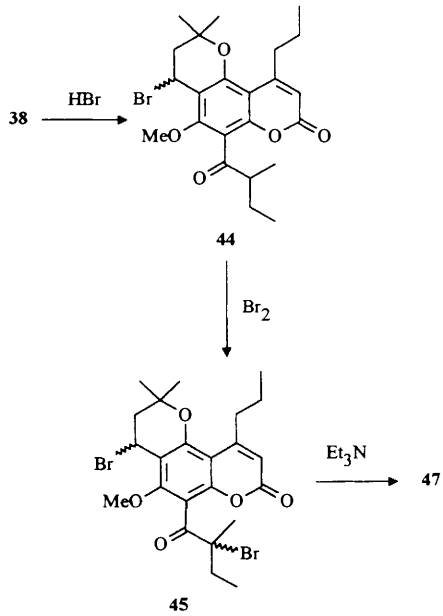
32 R = Ph
33 R = Pr
34 R = Me



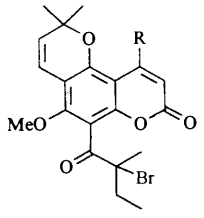
35 R^1 = Pr, R^2 = H
36 R^1 = Me, R^2 = H
37 R^1 = Ph, R^2 = Me
38 R^1 = Pr, R^2 = Me
39 R^1 = Me, R^2 = Me



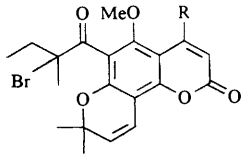
40 R^1 = Ph, R^2 = H
41 R^1 = Pr, R^2 = H
42 R^1 = Ph, R^2 = Me
43 R^1 = Pr, R^2 = Me



Scheme 1



46 R = Ph
47 R = Pr
48 R = Me



49 R = Ph
50 R = Pr

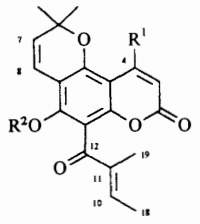
yields of 6- and 8-acyl coumarins in the 4-phenyl series,[26] and an alternative route was used for these compounds. 4-Phenyl-5,7-dihydroxy coumarin [prepared from Pechmann condensation of phloroglucinol (1,3,5-trihydroxybenzene) and ethyl benzoylacetate in 75% sulfuric acid],[27] was subjected to the Friedel–Crafts acylation/Fries rearrangement conditions previously described,[28] to afford 8- and 6-acyl coumarins **29** and **32** in 61% yield with an isomer ratio of *ca.* 7:4. Each pair of regioisomers was readily separated by fractional crystallisation or by chromatography as previously described.[26] Most importantly, the location of the acyl group in these series of coumarins has been established unequivocally by UV spectra analysis and by X-ray crystal structure determination.[26,29]

Introduction of the 2,2-dimethylpyrano ring was effected, in good to excellent yields (65–98%), by heating the appropriate coumarin (**29–33**) with 1,1-dimethoxy-3-methylbutan-3-ol in pyridine,[30] to afford the pyranocoumarins **5**, **35**, **36**, **40** and **41**. Ponnalide (also known as mammea A/BB cyclo D) **5** had been prepared and fully characterised previously.[26] The pyranocoumarins were O-alkylated with methyl iodide to afford the 5-methoxy coumarins **37–39**, **42** and **43** in yields of 54–99%. We thus had in hand the saturated acyl-side chain analogues of the *Calophyllum* coumarins **1–4**.

Introduction of α,β-unsaturation into the side chain proved to be quite difficult. After a number of methods had been investigated (see below), a 4-step hydrobromination–bromination–double dehydrobromination sequence converted the 2-methylbutanoyl side chain in **37–39**, **42** and **43** into the (*E*)-2-methylbut-2-enoyl (tigloyl) group to give coumarins **1**, **2**, **51**, **4** and **55**. Treatment of 5-methoxy coumarin **38** with hydrogen bromide gas in tetrachloromethane afforded the 4-bromo pyranocoumarin **44** (Scheme 1). Progress of the reaction could be monitored by ^{1}H NMR spectroscopy. Replacement of the two doublet signals at δ 5.65 and 6.50 for the olefinic protons in the pyran ring of **38** by a one-proton doublet of doublets at δ 5.55 and two separate one-proton doublet of doublet signals at δ 2.48 and 2.60, clearly indicating addition of HBr to form the 4-bromo-2,2-dimethylpyran ring system of **44**. This compound could not be isolated, due to its rapid decomposition with loss of HBr to reform pyranocoumarin **38**. However, immediate *in situ* treatment with one equiv. of bromine gave the dibromo coumarin **45**. As before, the reaction could be monitored by ^{1}H NMR spectroscopy. Loss of the doublet at δ 1.21 for the α-methyl (*Me*CHCO) of the acyl side chain, and its replacement by a singlet at δ 1.92 (MeCBrCO), together with the loss of the methine proton signal at δ 3.10 clearly indicated α-bromination of the 2-methylbutanoyl side chain. This compound too, was highly unstable and could not be isolated, however immediate treatment with triethylamine afforded the stable bromoacyl pyranocoumarin **47** in an overall yield from coumarin **38** of 81%. Similar treatment of the 5-methoxy coumarins **37**, **39**, **42** and **43** gave the corresponding bromoacyl pyranocoumarins **46**, **48–50** in overall yields of 44–95%.

While triethylamine readily dehydrobrominated the bromopyran function to regenerate the pyran ring, it failed to dehydrobrominate[31] the 2-bromo-2-methylbutanoyl side chain. Likewise, treatment with pyridine,[32] collidine (2,4,6-trimethylpyridine),[33] or silver nitrate in aqueous ethanol,[34] failed to effect the desired transformation. Finally, treatment of the bromoacyl pyranocoumarins **46–50** with 1,8-diazobicyclo[5.4.0]undec-7-ene (DBU),[35] afforded the (*E*)-2-methylbut-2-enoyl coumarins **1**, **2**, **51**, **4** and **55**, in yields of 36–71%.

Coumarin **1** is identical to calophyllolide isolated from the

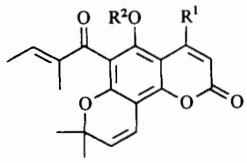


51 R^1 = Me, R^2 = Me

52 R^1 = Ph, R^2 = H

53 R^1 = Pr, R^2 = H

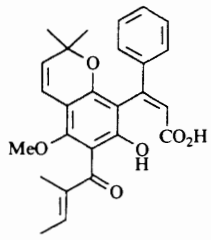
54 R^1 = Me, R^2 = H



55 R^1 = Pr, R^2 = Me

56 R^1 = Ph, R^2 = H

57 R^1 = Pr, R^2 = H



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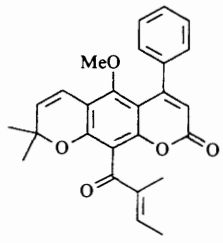

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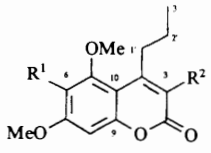
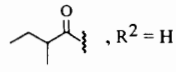
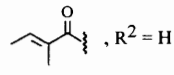
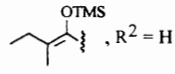
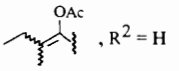
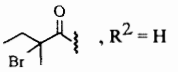


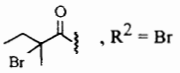
60 R^1 =  , R^2 = H

61 R^1 =  , R^2 = H

62 R^1 =  , R^2 = H

63 R^1 =  , R^2 = H

64 R^1 =  , R^2 = H

65 R^1 =  , R^2 = Br

seeds and bark of *C. inophyllum*,[2] and *C. bracteatum*,[3] confirming its proposed structure. We believe that the structure **58**, recently published as calophyllolide isolated from the leaves of *C. inophyllum* and the giant African snail,[14] is a typographical error. Coumarin **2** is identical in all respects to the unnamed natural product isolated from *C. inophyllum*.[4] Coumarin **51** on irradiation with UV light (254 nm) in hexane gave the (*Z*)-2-methylbut-2-enoyl (angeloyl) coumarin **3**. However examination of the spectral data revealed that this compound is not oblongulide isolated from *C. cordato-oblongum*.[5] Examination of the ^{1}H, ^{13}C and HETCOR NMR spectra of compounds **51** and **3** revealed that the structure proposed for oblongulide had been based on incorrect assignment of signals in the ^{13}C NMR spectrum by the authors.[5] In particular, signals attributed to the two methyl groups of the 2-methylbut-2-enoyl side chain (C-18 and C-19), and the C-13 methyl group were transposed (as were the signals assigned to the C-7 and C-8 olefinic carbons of the pyran ring, Table 1). The correct ^{13}C ($CDCl_3$, 75 MHz, δ/ppm) signals for the angeloyl chain in **3**, tigloyl chain in **51**, and 2-methylbut-2-enoyl group in natural oblongulide,[5] are: C-12 (194.5, 194.3, 193.5), C-11 (136.7, 139.9, 139.4), C-10 (137.4, 144.0, 143.0), C-18 (15.4, 15.2, 15.1) and C-19 (20.7, 10.7, 10.5). The correct structure for oblongulide, in agreement with the published ^{13}C and ^{1}H spectral data, is therefore coumarin **51** and not coumarin **3** as reported.[5]

Coumarin **4** is reported to be the structure of apetatolide isolated from *C. apetalum*.[6] However, the spectroscopic and physical data for coumarin **4** are not consistent with the spectroscopic and physical data for apetatolide. The assignment of structure **4** to apetatolide appears to be incorrect. We postulate the correct structure of apetatolide to be the linear pyranocoumarin **59**, although this remains to be proven by total synthesis.

A number of other methods were explored for introduction of α,β-unsaturation into the acyl side chain, using model systems. An attempt to dehydrogenate acyl coumarin **60** (prepared by methylation of coumarin **33**), directly to the α,β-unsaturated acyl coumarin **61** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ),[36–38] resulted in no reaction. Addition of a small amount of toluene-*p*-sulfonic acid (TSA) known to catalyse DDQ dehydrogenations,[39] resulted only in deacylation.§ Likewise an attempt to dehydrogenate coumarin **43** to the α,β-unsaturated acyl coumarin **55** with benzene seleninic anhydride,[40] was also unsuccessful. Trialkylsilyl enol ethers are converted into α,β-unsaturated carbonyl compounds readily by DDQ,[41,42] however attempts to form the trimethylsilyl enol ether **62** with trimethylsilyl chloride and either triethylamine or lithium diisopropylamide[43] failed. Likewise attempts to prepare the α-bromo acyl coumarins *via* the ketone enolates,[44] also failed as the lithium enolate could not be prepared by the standard procedures. Attempts to form the enol acetate **63** with isopropenyl acetate and sulfuric acid as catalyst again led to deacylation of **60**, but using TSA as catalyst the enol acetate **63** could be formed (as a mixture of *cis* and *trans* isomers), in low yield.[45] It was intended that the enol acetate **63** should provide access to the desired enolate anion,[46] however this approach was abandoned when another eventually successful approach was developed. Attempts to α-hydroxylate coumarin **60** using [bis(trifluoroacetoxy)iodo]benzene,[47] were also unsuccessful.

Following reports that copper(II) bromide will selectively brominate ketones and acylated phenol derivatives α to the carbonyl,[48–50] acyl coumarin **30** was treated with this reagent. Unfortunately, bromination occurred exclusively on the aromatic ring to afford 6-bromo coumarin **66** in good yield. Treatment of acyl coumarin **30** with bromine in glacial acetic acid,[51] gave the same result. Radical bromination of coumarin **37** with NBS (*N*-bromosuccinimide),[52] resulted in bromination of the pyran ring rather than acyl bromination. Treatment of acyl coumarin **60** with bromine in tetrachloromethane was partially successful, resulting in a mixture of the desired bromoacyl coumarin **64** and dibrominated coumarin **65**.¶ Likewise, treatment of pyranocoumarin **67** (prepared by hydrogenation of pyranocoumarin **38**), afforded a mixture of the mono- and di-brominated coumarins **68** and **69**. Fortunately, it was found that addition of a little hydrogen bromide gas prior to addition of bromine led to the exclusive formation of bromoacyl coumarin **68**. This latter result led to the successful method described above. Presumably, hydrogen

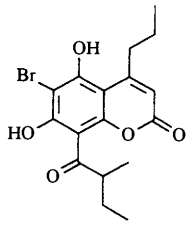
§ Acid-catalysed retro-Friedel–Crafts acylations are well known in these series of compounds.[26,32]

¶ Bromination of coumarins at C-3 is not uncommon.[53,54]

Table 1 ^{13}C NMR data[a] for compounds **1–3**, **7–9**, **13–15**, **17–19**, **21**, **24–26**, **51**, **79–81** and **84**

Carbon[b]	**1**	**2**	**51**	**3**	**7**	**8**	**9**	**79**[c]	**80**[c]	**81**[c]	**24**	**25**	**84**[c]	**26**	**13**	**14**	**17**	**18**	**19**	**21**	**15**
2	159.5	159.8	159.6	159.4	159.5	159.4	159.6	159.9	159.7	159.9	160.3	160.8	160.7	160.5	160.1	160.5	160.3	160.7	161.0	160.9	160.0
3	114.2	112.7	113.3	113.4	113.4	113.4	111.9	111.2	112.8	111.3	111.4	110.2	110.9	111.9	111.5	110.1	111.7	111.7	110.3	111.8	110.9
4	155.0	157.2	153.4	153.3	154.9	154.9	157.0	157.9	155.7	157.9	156.4	159.0	158.5	156.3	156.4	158.9	155.0	156.3	158.8	154.9	157.8
4a	105.6	106.2	106.8	106.8	103.9	103.9	104.3	102.5	101.8	102.5	103.3	103.8	103.4	103.4	103.6	104.0	104.6	103.0	103.5	104.1	104.1
4b	151.7	152.1	151.7	151.6	155.6	155.7	155.9	159.7	160.1	160.4	151.0	151.3	152.6	151.1	150.9	151.1	151.6	151.1	151.4	151.8	151.8
6	77.4	78.0	77.9	78.0	78.6	78.6	79.2	77.3	78.9	79.8	76.9	77.7	75.5	77.1	77.0	77.6	77.6	77.0	77.6	77.5	77.8
7	129.0	128.6	128.8	128.8	127.4	127.4	126.9	45.5	47.0	47.0	127.3	126.9	35.0	127.2	127.4	126.9	127.2	127.3	126.8	126.9	126.8
8	116.0	116.5	116.4	116.4	115.2	115.2	115.7	192.6	191.3	191.3	116.0	116.7	64.9	115.9	115.9	116.5	116.4	116.0	116.5	116.5	116.3
8a	110.7	110.7	110.8	111.2	105.4	105.4	105.4	106.6	107.3	107.4	106.4	106.6	109.1	106.0	106.3	106.3	106.4	106.1	106.3	106.2	106.2
8b	155.8	155.2	155.3	155.3	159.4	159.4	158.8	157.3	157.8	157.1	152.6	152.1	150.5	153.9	153.7	153.1	153.2	153.7	153.1	153.2	152.7
10	144.2	144.0	144.0	137.4	79.6	77.3	77.1	78.7	78.9	78.9	75.8	75.8	78.8	71.2	77.2	77.1	77.2	73.0	73.0	73.0	76.5
11	139.9	139.8	139.9	136.7	47.2	45.9	45.8	127.9	128.0	128.0	35.6	35.7	126.8	37.2	40.4	40.4	40.4	38.2	38.2	38.2	38.1
12	194.3	194.3	194.3	194.5	190.0	191.6	191.4	114.9	114.9	115.0	62.9	63.0	115.6	64.6	67.1	67.1	67.2	61.8	61.8	61.7	67.1
12a	115.0	115.3	115.2	117.9	103.3	102.8	102.8	103.9	103.8	104.0	105.5	105.8	102.7	103.9	106.1	106.4	106.3	106.1	106.1	106.2	101.1
12b	152.0	152.2	152.7	153.0	155.1	155.4	155.7	154.0	154.8	154.1	154.2	154.6	154.6	154.6	154.1	154.5	154.1	153.5	153.9	153.4	154.4
13	127.3	38.4	24.4	24.4	127.2	127.2	38.7	38.8	126.8	38.8	127.2	38.7	38.8	127.3	127.3	38.6	24.5	127.2	38.6	24.4	38.5
13a	139.5	—	—	—	139.8	139.8	—	—	139.8	—	140.0	—	—	139.9	139.9	—	—	140.0	—	—	—
14	127.5	23.0	—	—	127.5	127.5	23.1	22.9	127.7	22.9	127.3	23.3	23.1	127.4	127.4	23.2	—	127.3	23.3	—	23.2
15	127.8	13.9	—	—	127.7	127.7	13.8	13.8	128.0	13.8	127.5	14.1	13.9	127.6	127.6	14.0	—	127.6	14.0	—	14.0
16	26.9	27.7	27.8	27.7	27.2	27.3	28.0	27.9	28.1	28.0	26.8	27.8	28.1	26.9	26.6	27.4	27.4	26.8	27.7	27.6	27.7
17	26.9	27.7	27.8	27.7	27.4	27.4	28.2	28.0	28.3	28.3	26.8	27.8	28.3	26.9	27.0	28.0	28.0	26.9	27.8	27.8	27.9
18	15.2	15.1	15.2	15.4	19.6	16.0	15.9	15.8	18.5	19.5	16.2	16.2	16.7	17.6	18.9	18.9	18.9	18.8	18.8	18.8	19.1
19	10.7	10.7	10.7	20.7	10.5	9.2	9.1	8.9	9.5	9.8	9.6	9.7	7.2	9.1	15.1	15.1	15.1	12.5	12.5	12.5	15.2
OMe	63.0	63.0	63.0	63.2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
OCO	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	170.7
OCO*Me*	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	21.1

[a] Spectra were recorded in $CDCl_3$. [b] See text for carbon numbering system used. [c] Note that compounds **79**, **80**, **81** and **84** belong to the alternative regioisomer series and so carbons 6, 7 and 8, and 10, 11 and 12 appear in reverse order for these compounds due to the numbering system used, *e.g.*, carbons 6, 7 and 8 in compound **25** correspond to carbons 10, 11 and 12 in compound **84**.



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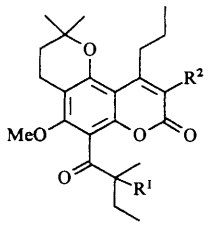
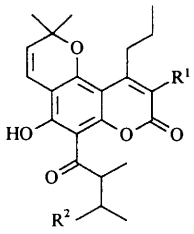


67 R^1 = H, R^2 = H

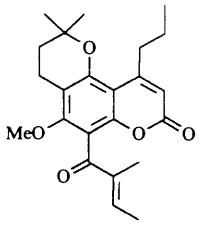
68 R^1 = Br, R^2 = H

69 R^1 = Br, R^2 = Br



70 R^1 = Br, R^2 = H

72 R^1 = H, R^2 = Br



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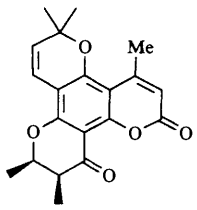
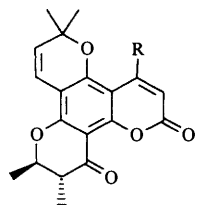


73



74 R = Pr

75 R = Me

bromide activates the acyl group towards bromination *via* enol formation, although it was also found that excessive addition of hydrogen bromide or a prolonged reaction time would again cause deacylation. Interestingly, the hydrobromination–bromination–dehydrobromination sequence when applied to coumarin **35** resulted in the exclusive formation of the 3-bromo coumarin **70**. Bromoacyl coumarin **68** could be dehydrobrominated to the α,β-unsaturated acyl coumarin **71** with DBU, but unfortunately attempts to dehydrogenate this compound to **2** were unsuccessful.

Demethylation of the 5-methoxy coumarins **1**, **2** and **51** was achieved in almost quantitative yields with magnesium iodide–diethyl ether,[55] to afford the corresponding 5-hydroxy coumarins **52–54**. Demethylation of **2** with boron tribromide,[56] could also be effected but usually led to the isolation of substantial amounts of 3-bromo-2-methylbutanoyl coumarin **72**. Similar demethylation of the 5-methoxy coumarins **4** and **55** could not be achieved with magnesium iodide–diethyl ether or boron tribromide, as in these cases destruction of the pyran ring occurred. Demethylation with these Lewis acid reagents is facilitated by chelation with an acyl group. In the case of coumarins **1**, **2** and **51** only cleavage of the methoxy group can be aided by acyl group chelation. However, in the regioisomers **4** and **55** both cleavage of the methyl ether and cleavage of the chromene ether is aided by chelation. Consequently, other demethylation agents were examined. The hindered borane B-bromo-9-BBN,[57] and trimethylsilyl iodide,[58,59] were ineffective in causing demethylation. However, boron tribromide–dimethyl sulfide complex in dichloromethane,[60] gave selective cleavage to afford 5-hydroxy coumarins **56** and **57**, although in modest to moderate yields (15–50%).‖

Treatment of the 5-hydroxy coumarins **52–54** with triethylamine resulted in cyclisation of the acyl group to afford mixtures of the (±)-*cis* and (±)-*trans*-2,3-dimethyl chromanones **8** and **7**, **9** and **74**, and **73** and **75**, respectively, in high yield (overall 95–98%). Ratios of *cis* and *trans* isomers obtained were usually approximately 1:1 or slightly favoured the *trans* isomer. Each pair of *cis* and *trans* isomers were readily separated by chromatography. From the cyclisation reaction of **52** a very small quantity (1.5%) of the isomeric coumarins **76** and **77** were also isolated along with the cyclised products **7** and **8**. These appear to be formed by iodine-catalysed isomerisation of the acyl olefinic bond during the demethylation of **52** with magnesium iodide–diethyl ether, and are not cyclised under subsequent treatment with triethylamine.

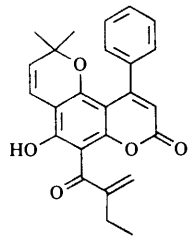
The spectral data for (±)-*trans*-chromanone **7** and (±)-*cis*-chromanone **8** are in excellent agreement with that published for inophyllum C and inophyllum E, respectively, isolated from *C. inophyllum*.[10,14] (±)-*cis*-Chromanone **9**, previously prepared by another route,[61] is claimed to be the structure of calanolide D isolated from *C. lanigerum*.[11] Our synthesis of *cis*-chromanone **9** reveals that the physical and spectral properties for this compound are in complete agreement with those of the same compound recently synthesised.[61] However, careful examination of the spectral data for this compound and calanolide D[11] has shown that they are not the same compound. Comparison of the ^{1}H NMR spectra for these two compounds shows clear differences in the chemical shifts for several proton signals. In particular, the doublet signal for the C-8 pyran ring proton in chromanone **9** appears at δ 6.63. However, the signal for the same proton in calanolide D appears at δ 6.78. Minor differences are also observed, in the chemical shifts for the C-18 methyl group, the C-3 and C-7 olefinic protons, and in the splitting pattern for the C-13 methylene group. In the ^{13}C NMR spectra (Table 1), minor differences in the chemical shifts (~ 1–2 ppm) for several carbon signals are discernible. Therefore the structure proposed for calanolide D is in error. Our experience in this area led us to believe that calanolide D was probably the corresponding regioisomer of **9**, that is *cis* chromanone **79**.**

Accordingly, 5-hydroxy coumarins **56** and **57** were cyclised with triethylamine to afford mixtures of the corresponding (±)-*cis*- and (±)-*trans*-2,3-dimethylchromanones **78** and **80**, and **79** and **81**.†† Ratios of *cis* and *trans* isomers obtained were usually 1:1 or slightly favoured the *cis* isomer. Each pair of *cis* and *trans* isomers was separated by chromatography. The ^{1}H and

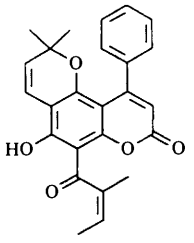
‖ Protecting groups other than methyl were examined in this series but of those that would survive the hydrobromination–bromination–dehydrobromination sequence, none could be cleaved selectively in the presence of the pyran or other functionality in the molecule.

** In the ^{1}H NMR ($CDCl_3$) spectra for related coumarins of this class, the doublet signal for the proton at position C-8 on the pyran ring, typically appear at δ ~ 6.60 in those coumarins where the pyran ring is fused at C-5 and C-6 of the coumarin ring. Whereas in those coumarins where the pyran ring is fused at C-7 and C-8, the doublet signal for the proton at C-8 on the pyran ring typically appears at δ ~ 6.80.

†† On one occasion, from the cyclisation reaction of chromanone **57** a small amount of the isomeric coumarin **82** was isolated along with **79** and **81**.



76



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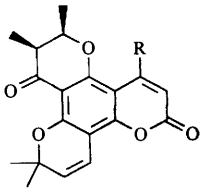
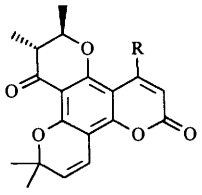


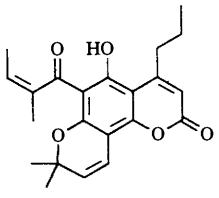
78 R = Ph

79 R = Pr

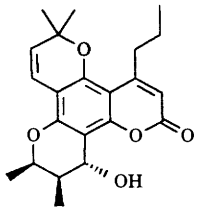


80 R = Ph

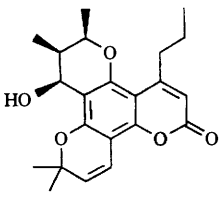
81 R = Pr



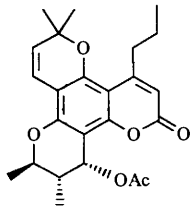
82



83



84



85

^{13}C spectral data for (±)-*cis*-chromanone **79** are in complete agreement with that for calanolide D. Therefore, the correct structure of calanolide D is chromanone **79** and not chromanone **9**, as previously reported.‡‡[11,61] (±)-*trans*-Chromanones **80** and **81** have physical and spectral data in good agreement with that published for tomentolide A and tomentolide B, respectively, both isolated from *C. tomentosum*.[6] The previously unknown stereochemistry about the 2,3-dimethyl chromanone ring of both compounds is therefore now established as being *trans*.

Sodium boranuide reduction (a buffered system was used to prevent *cis*/*trans* isomerisation of the starting material) of chromanones **8** and **9** afforded mixtures of (±)-chromanol epimers **24** and **26**, and **25** and **83**, respectively, in good yields (overall 52–75%). Epimer ratios were 50:1 and 30:1, respectively, reflecting the more favoured approach of hydride to the least hindered face of the *cis*-2,3-dimethylchromanone ring. Each epimer pair was separable by chromatography. The physical and spectral data for chromanols (±)-**24** and (±)-**26** are in complete agreement with those published for inophyllum A and inophyllum D, respectively, isolated from *C. inophyllum*,[10,14] and *C. moonii*.[16] (±)-Chromanol **25**, previously prepared by another route,[61] is claimed to be the structure of calanolide C isolated from *C. lanigerum*.[11] The physical and spectral data for (±)-chromanol **25** prepared in our study are in good agreement with those for the same compound recently synthesised.[61] However, careful examination of the spectral data for (±)-chromanol **25** and calanolide C,[11] has shown that they are not the same compound. Comparison of the ^1H NMR spectra for these two compounds shows very clear differences in the chemical shifts for several proton signals. In particular, the doublet signals for the C-8 pyran proton and the C-19 methyl group in (±)-chromanol **25** appear at δ 6.63 and 1.15, respectively. However, these signals for the same protons in calanolide C appear at δ 6.83 and 1.06, respectively. Differences are also observed in the chemical shifts for the C-15 methyl group, the C-10 and C-11 chromanol ring protons, and in the splitting patterns for the C-10, C-11 protons and the C-13 methylene group. In addition the C-16 and C-17 methyl groups on the pyran ring in (±)-chromanol **25** appear as a six-proton singlet at δ 1.49 as opposed to 2 three-proton singlets at δ 1.46 and 1.52 in calanolide C. In the ^{13}C NMR spectra (Table 1), minor differences in the chemicals shifts of several carbon signals are also readily discernible. Therefore the structure assigned to calanolide C is incorrect. As in the case of calanolide D, we suspected that the true structure of calanolide C was probably the corresponding regioisomer **84**.§§ Accordingly, (±)-*cis*-chromanone **79** was reduced with buffered sodium boranuide to afford (±)-chromanol **84** in good yield (73%). In this case none of the corresponding C-8 epimer could be detected. (±)-Chromanol **84** has identical spectroscopic data as that reported for calanolide C, thereby establishing the correct structure of calanolide C as **84** and not as **25** as reported.‡‡[11,61]

Sodium boranuide reduction of (±)-chromanones **7**, **74** and **75** afforded mixtures of the corresponding (±)-chromanol epimers **13** and **18**, **14** and **19**, and **17** and **21** in overall yields of 49–58%, with epimer ratios of approximately 1:1. Each isomer pair was separated by chromatography. The spectral data for (±)-chromanol **13** are in complete agreement with the data published for inophyllum B.¶¶[10,14] (±)-Chromanol **18** is as such a mixture of (+)-chromanol **18** (assigned to inophyllum P) and (−)-chromanol **22** (assigned to soulattrolide). The physical and spectral data for (±) chromanol **18** and **22** are in complete agreement with the data published for inophyllum P and soulattrolide.¶¶[14,15] The spectral data for (±)-chromanol **14** are identical with that for natural calanolide A,[11] and (±)-

‡‡ Dr G. B. Dreyer has informed us in a personal communication that he has reached the same conclusion.

§§ Apparently, the possibility that calanolides C and D might not belong to the same regioisomer series as calanolides A and B was not previously considered, despite differences in the ^1H NMR signals for the C-8 and C-19 protons for these compounds.[11] A discrepancy in the ^1H NMR between natural calanolide C and the synthetic (±)-chromanol **25** was noted, however, this was attributed to either an artifact or a typographical error.[61]

¶¶ In reference 14, we believe the ^{13}C NMR data for inophyllum B and inophyllum P in the table have been accidentally transposed.

calanolide A previously synthesised by another route.[61] (±)-Chromanol **19** is as such a mixture of (+)-chromanol **19** (assigned to calanolide B) and (−)-chromanol **22** (assigned to costatolide). The physical and spectral data for (±)-chromanol **19** and **23** are in good agreement with that of calanolide B[11] and costatolide.‖‖[17,18] The ^{1}H NMR spectral data for (±)-chromanol **17** and (±)-chromanol **21** are in good agreement with those for cordatolide A and cordatolide B, respectively, isolated from *C. cordato-oblongum*.[5] The ^{13}C NMR data for (±)-chromanol **21** (Table 1), are in good agreement with that published for cordatolide B.*** However, as in the case of oblongulide some of the signals have been incorrectly assigned for the natural material. In particular, the signals for the chromene olefinic carbons at C-7 and C-8 have been switched, as have the C-4 and C-19 methyl signals and those for C-10 and C-12 methine carbons.†††[5]

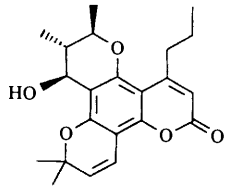
Sodium boranuide reduction of (±)-chromanone **81** afforded a mixture of readily separable chromanol epimers **86** and **87**, thereby completing the series. Finally, (±)-chromanols **14** and **19** were acetylated with acetic anhydride to give (±)-12-acetoxychromanol **15** and (±)-12-acetoxychromanol **85**, respectively. The spectral data for (±)-12-acetoxychromanol **15** are identical to that for 12-acetoxycalanolide A isolated from *C. lanigerum*.[11]

Experimental

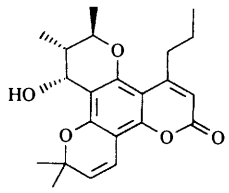
Unless otherwise stated the following generalisations apply. ^{1}H NMR spectra were recorded in $CDCl_3$ using a 300 MHz Varian Gemini 300 spectrometer. Chemical-shift values (δ relative to $SiMe_4$) were assigned using residual $CHCl_3$ as the internal standard. *J*-Values are given in Hz. ^{13}C NMR spectra were recorded in $CDCl_3$ using a Gemini 300 spectrometer operating at 75 MHz, with broad-band decoupling. Chemical-shift values (δ relative to $SiMe_4$) were assigned using $CDCl_3$ as the internal standard. Primary, secondary, tertiary and quaternary carbons were assigned by use of DEPT, HETCOR and LRHETC pulse sequences and by analogy. For ease of comparison, the carbon numbering system used for reporting spectral data of the pyranocoumarins is that used previously[11,14] for the natural materials. Otherwise standard nomenclature is used. High resolution mass spectra were recorded on a VG ProSpec instrument. Low resolution mass spectra were recorded on a Finnigan SSQ 710 instrument. Mps were determined using a Yanako hot stage micro melting point apparatus MP-S3 and are uncorrected. Analytical TLC was performed on 5 × 2 cm Silica gel HF_{254} coated (0.25 mm) plates, inspected under UV light, or visualised by conc. sulfuric acid–*p*-anisaldehyde spray or potassium permanganate spray reagents. All new compounds gave a single spot by TLC.

5,7-Dihydroxy-6 and 8-(2-methylbutanoyl)-4-phenyl-2*H*-chromen-2-ones 32 and 29

These coumarins were prepared from 5,7-dihydroxy-4-phenyl coumarin,[27] and 2-methylbutanoyl chloride using the Friedel–Crafts acylation/Fries rearrangement procedure previously described.[28] Chromatography on silica, with dichloromethane and then dichloromethane–methanol (99:1 v/v) as eluent gave the 8-acyl coumarin **29** (39%) and then the 6-acyl coumarin **32** (22%). Both compounds were identical in all respects with authentic samples prepared by another route.[26]



86



87

5,7-Dihydroxy-6 and 8-(2-methylbutanoyl)-4-propyl-2*H*-chromen-2-ones 33 and 30

These were prepared from (2-methylbutanoyl)-1,3,5-trihydroxybenzene and ethyl 3-oxohexanoate as previously described.[26]

5,7-Dihydroxy-4-methyl-6 and 8-(2-methylbutanoyl)-2*H*-chromen-2-ones 34 and 31

These were prepared from (2-methylbutanoyl)-1,3,5-trihydroxybenzene and ethyl acetoacetate as previously described.[26,32]

Preparation of the pyranocoumarins 5, 35, 36, 40 and 41

A mixture of the appropriate 4-alkyl or aryl-5,7-dihydroxy-6 or 8-(2-methylbutanoyl)coumarin (1 mol equiv.) and 1,1-dimethoxy-3-methylbutan-3-ol[30] (4 mol equiv.) in pyridine (5 cm^3) was stirred and heated to 160 °C under an air condenser for 48 h. The residue was allowed to cool and then was chromatographed on a silica column, eluting with hexane–dichloromethane, to give the product. Using this method the following coumarins were prepared:

Ponnalide 5. This was prepared from 5,7-dihydroxy-8-(2-methylbutanoyl)-4-phenyl-2*H*-chromen-2-one **29** (9.0 g, 27 mmol) as yellow crystals (10.6 g, 98%), mp 126–127 °C (from hexane–dichloromethane) (lit.,[26] 127–129 °C); δ_H 0.95 and 0.97 (6 H, 2 s, Me_2C), 1.03 (3 H, t, *J* 7.4, *Me*CH_2CH), 1.29 (3 H, d, *J* 6.7, *Me*CHCO), 1.44–1.57 and 1.88–2.01 (2 H, 2 m, MeCH_2CH), 3.91–4.01 (1 H, m, *J* 6.7, MeC*H*CO), 5.39 (1 H, d, *J* 10.0, ArCH=C*H*), 6.02 (1 H, s, C=CHCO), 6.63 (1 H, d, *J* 10.0, ArCH=C*H*), 7.20–7.42 (5 H, m, arom.) and 14.50 (1 H, s, OH).

5-Hydroxy-2,2-dimethyl-6-(2-methylbutanoyl)-10-propyl-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*']dipyran-8-one 35. This was prepared from 5,7-dihydroxy-8-(2-methylbutanoyl)-4-propylcoumarin **30** (21.5 g, 71 mmol) as pale yellow crystals (24.6 g, 94%), mp 93–94 °C (from hexane–dichloromethane) (lit.,[26] 94–96 °C); δ_H 0.93 (3 H, t, *J* 7.4, *Me*CH_2CH), 1.00 (3 H, t, *J* 7.3, *Me*CH_2CH_2), 1.20 (3 H, d, *J* 6.6, *Me*CHCO), 1.31–1.47 and 1.77–1.91 (2 H, 2 m, MeCH_2CH), 1.49 (6 H, s, Me_2C), 1.53–1.68 (2 H, m, MeCH_2CH_2), 2.86 (2 H, m, $MeCH_2CH_2$), 3.80–3.90 (1 H, m, *J* 6.7, MeC*H*CO), 5.53 (1 H, d, *J* 10.0, ArCH=C*H*), 5.96 (1 H, s, C=CHCO), 6.67 (1 H, d, *J* 10.0, ArC*H*=CH) and 14.41 (1 H, s, OH).

5-Hydroxy-2,2,10-trimethyl-6-(2-methylbutanoyl)-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*']dipyran-8-one 36. This was prepared from 5,7-dihydroxy-4-methyl-8-(2-methylbutanoyl)-2*H*-chromen-2-one **31** (5.0 g, 18 mmol) as yellow crystals (4.88 g, 79%), mp 74–75 °C (from hexane–dichloromethane) (Found: M^+, 342.1467. $C_{20}H_{22}O_5$ requires *M*, 342.1467); δ_H 0.98 (3 H, t, *J* 7.3, *Me*CH_2CH), 1.24 (3 H, d, *J* 6.7, *Me*CHCO), 1.41–1.52 and 1.84–1.93 (2 H, 2 m, MeCH_2CH), 1.53 (6 H, s, Me_2C), 2.59 (3 H, s, *Me*C=CHCO), 3.84–3.95 (1 H, m, *J* 6.7, MeC*H*CO), 5.57 (1 H, d, *J* 10.0, ArCH=C*H*), 5.99 (1 H, s, MeC=C*H*CO), 6.71 (1 H, d, *J* 10.0, ArC*H*=CH) and 14.50 (1 H, s, OH); δ_C 11.7 (CH_3, C-18), 16.5 (CH_3, C-19), 25.0 (CH_3, C-13), 27.1 (CH_2, C-10), 28.2

‖‖ The quality of the published ^{1}H NMR spectrum for natural costatolide in reference 17 does not permit a complete comparison with the ^{1}H NMR spectrum of synthetic (±) costatolide to be made. However we are inclined to believe that the structure of costatolide is correct based on the comparisons made with natural and synthetic analogues cited in references 10, 17 and 18.

*** In reference 5, it appears that the ^{13}C NMR data for cordatolide B in the figure has been titled accidentally as belonging to cordatolide A.

††† In reference 5, we believe the reported melting points for oblongulide and cordatolide A may have been accidentally transposed.

(CH_3, C-16), 28.2 (CH_3, C-17), 46.8 (CH, C-11), 79.5 (C, C-6), 103.3 (C, C-4a), 103.8 (C, C-8a), 106.1 (C, C-12a), 111.1 (CH, C-3), 115.8 (CH, C-8), 126.5 (CH, C-7), 154.6 (C, C-4), 156.6 (C, C-4b), 156.9 (C, C-12b), 159.0 (C, C-2), 163.3 (C, C-8b) and 210.6 (C, C-12); *m/z* 342 (M^+, 48%), 327 (100), 309 (44) and 285 (80).

5-Hydroxy-8,8-dimethyl-6-(2-methylbutanoyl)-4-phenyl-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*']dipyran-2-one 40. This was prepared from 5,7-dihydroxy-6-(2-methylbutanoyl)-4-phenyl-2*H*-chromen-2-one **32** (7.38 g, 22 mmol) as a yellow solid (5.75 g, 65%), mp 84–87 °C (lit.,[62] 89.5–92 °C); δ_H 0.91 (3 H, t, *J* 7.4, *Me*CH_2CH), 1.17 (3 H, d, *J* 7.0, *Me*CHCO), 1.34–1.50 and 1.77–1.92 (2 H, 2 m, MeCH_2CH), 1.56 and 1.58 (6 H, 2 s, Me_2C), 3.66–3.78 (1 H, m, *J* 7.0, MeC*H*CO), 5.64 (1 H, d, *J* 10.1, ArCH=CH), 6.00 (1 H, s, C=CHCO), 6.91 (1 H, d, *J* 10.1, ArC*H*=CH), 7.30–7.43 (5 H, m, arom.) and 14.70 (1 H, s, OH).

5-Hydroxy-8,8-dimethyl-6-(2-methylbutanoyl)-4-propyl-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*']dipyran-2-one 41. This was prepared from 5,7-dihydroxy-6-(2-methylbutanoyl)-4-propyl-2*H*-chromen-2-one **33** (18.2 g, 60 mmol) as yellow crystals (18.25 g, 82%), mp 99–100 °C (from hexane–dichloromethane) (lit.,[26] 97–98 °C); δ_H 0.90 (3 H, t, *J* 7.4, *Me*CH_2CH), 0.97 (3 H, t, *J* 7.3, *Me*CH_2CH_2), 1.17 (3 H, d, *J* 6.8, *Me*CHCO), 1.37–1.48 and 1.80–1.91 (2 H, 2 m, MeCH_2CH), 1.51 (6 H, 2 s, Me_2C), 1.55–1.68 (2 H, m, MeCH_2CH_2), 2.91 (2 H, m, $MeCH_2CH_2$), 3.67–3.78 (1 H, m, *J* 6.7, MeC*H*CO), 5.56 (1 H, d, *J* 10.1, ArCH=C*H*), 5.92 (1 H, s, C=CHCO), 6.80 (1 H, d, *J* 10.1, ArC*H*=CH) and 15.27 (1 H, s, OH).

Preparation of the 5-methoxy pyranocoumarins 37–39, 42 and 43

A mixture of the appropriate hydroxy coumarin (1 mol equiv.), methyl iodide (1.5 mol equiv.), and anhydrous potassium carbonate (6 equiv.) in dry acetone (150 cm^3) was stirred and heated to reflux overnight. The cooled solution was filtered through a bed of Celite and the solvents were evaporated. The residue was chromatographed on flash column silica gel with hexane–ethyl acetate (9:1 v/v) as eluent to afford the methoxy derivative. Using this method the following coumarins were prepared:

5-Methoxy-2,2-dimethyl-6-(2-methylbutanoyl)-10-phenyl-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*']dipyran-8-one 37. This was prepared from ponnalide **5** (9.0 g, 22.2 mmol) as a yellow gum (8.44 g, 91%) (Found: M^+, 418.1766. $C_{26}H_{26}O_5$ requires *M*, 418.1780); δ_H 0.97 (6 H, 2 s, Me_2C), 1.01 (3 H, t, *J* 7.4, *Me*CH_2CH), 1.24 (3 H, d, *J* 6.9, *Me*CHCO), 1.43–1.57 and 1.83–1.96 (2 H, 2 m, MeCH_2CH), 3.01–3.12 (1 H, m, *J* 7.0, MeC*H*CO), 3.81 (3 H, s, MeO), 5.50 (1 H, d, *J* 10.0, ArCH=C*H*), 6.06 (1 H, s, C=CHCO), 6.44 (1 H, d, *J* 10.0, ArC*H*=CH), 7.23–7.26 and 7.38–7.41 (5 H, 2 m, arom.); δ_C 11.6 (CH_3, C-18), 14.9 (CH_3, C-19), 25.2 (CH_2, C-10), 26.9 (CH_3, C-16), 26.9 (CH_3, C-17), 49.1 (CH, C-11), 64.0 (MeO), 77.5 (C, C-6), 105.8 (C, C-4a), 111.2 (C, C-8a), 114.4 (CH, C-3), 115.9 (CH, C-8), 117.6 (C, C-12a), 127.2 (CH, C-13), 127.5 (CH, C-14), 127.8 (CH, C-15), 129.2 (CH, C-7), 139.5 (C, C-13a), 151.6 (C, C-12b), 152.5 (C, C-4b), 155.0 (C, C-4), 156.1 (C, C-8b), 159.1 (C, C-2) and 205.7 (C, C-12); *m/z* 418 (M^+, 18%), 403 (45), 362 (38) and 361 (100).

5-Methoxy-2,2-dimethyl-6-(2-methylbutanoyl)-10-propyl-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*']dipyran-8-one 38. This was prepared from 5-hydroxy coumarin **35** (3.5 g, 9.5 mmol) as an oil (3.6 g, 99%), which on standing gave pale yellow crystals, mp 86.5–88.5 °C (Found: M^+, 384.1934. $C_{23}H_{28}O_5$ requires *M*, 384.1937); δ_H 0.94 (3 H, t, *J* 7.5, *Me*CH_2CH), 1.01 (3 H, t, *J* 7.3, *Me*CH_2CH_2), 1.16 (3 H, d, *J* 6.9, *Me*CHCO), 1.38–1.50 and 1.78–1.85 (2 H, 2 m, MeCH_2CH), 1.49 (6 H, 2 s, Me_2C), 1.57–1.67 (2 H, m, MeCH_2CH_2), 2.87 (2 H, m, *J* 7.6, $MeCH_2CH_2$), 2.93–3.01 (1 H, m, *J* 6.9, MeC*H*CO), 3.77 (3 H, s, MeO), 5.65 (1 H, d, *J* 10.0, ArCH=C*H*), 5.99 (1 H, s, C=CHCO) and 6.50 (1 H, d, *J* 10.0, ArC*H*=CH); δ_C 11.4 (CH_3, C-18), 13.8 (CH_3, C-15), 14.8 (CH_3, C-19), 23.0 (CH_2, C-14), 25.1 (CH_2, C-10), 27.6 (CH_3, C-16), 27.7 (CH_3, C-17), 38.4 (CH_2, C-13), 49.0 (CH, C-11), 63.9 (MeO), 78.1 (C, C-6), 106.4 (C, C-4a), 111.1 (C, C-8a), 112.7 (CH, C-3), 116.3 (CH, C-8), 117.8 (C, C-12a), 128.7 (CH, C-7), 151.9 (C, C-12b), 152.6 (C, C-4b), 155.4 (C, C-8b), 157.2 (C, C-4),. 159.3 (C, C-2) and 205.8 (C, C-12); *m/z* 384 (M^+, 61%), 369 (57), 351 (100), 328 (70) and 327 (96).

5-Methoxy-2,2,10-trimethyl-6-(2-methylbutanoyl)-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*']dipyran-8-one 39. This was prepared from 5-hydroxy coumarin **36** (11.29 g, 33 mmol) as white needles (10.9 g, 93%), mp 97–100 °C (from hexane–dichloromethane) (Found: M^+, 356.1619. $C_{21}H_{24}O_5$ requires *M*, 356.1624); δ_H 0.97 (3 H, t, *J* 7.4, *Me*CH_2CH), 1.19 (3 H, d, *J* 6.9, *Me*CHCO), 1.41–1.50 and 1.78–1.91 (2 H, 2 m, MeCH_2CH), 1.51 and 1.52 (6 H, 2 s, Me_2C), 2.58 (3 H, s, *Me*C=CHCO), 2.94–3.05 (1 H, m, *J* 6.9, MeC*H*CO), 3.80 (3 H, s, MeO), 5.67 (1 H, d, *J* 10.0, ArCH=C*H*), 6.02 (1 H, s, MeC=C*H*CO) and 6.53 (1 H, d, *J* 10.0, ArC*H*=CH); δ_C 11.6 (CH_3, C-18), 14.9 (CH_3, C-19), 24.4 (CH_3, C-13), 25.2 (CH_2, C-10), 27.8 (CH_3, C-16), 27.8 (CH_3, C-17), 49.1 (CH, C-11), 64.0 (MeO), 78.0 (C, C-6), 107.0 (C, C-4a), 111.3 (C, C-8a), 113.4 (CH, C-3), 116.4 (CH, C-8), 117.7 (C, C-12a), 128.9 (CH, C-7), 151.6 (C, C-12b), 153.1 (C, C-4b), 153.4 (C, C-4), 155.5 (C, C-8b), 159.3 (C, C-2) and 205.8 (C, C-12); *m/z* 356 (M^+, 11%), 341 (13), 300 (18) and 299 (100).

5-Methoxy-8,8-dimethyl-6-(2-methylbutanoyl)-4-phenyl-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*']dipyran-2-one 42. This was prepared from 5-hydroxy coumarin **40** (2.94 g, 7.3 mmol) as a yellow gum (1.64 g, 54%) (Found: M^+, 418.1780. $C_{26}H_{26}O_5$ requires *M*, 418.1780); δ_H 0.95 (3 H, t, *J* 7.4, *Me*CH_2CH), 1.14 (3 H, d, *J* 7.0, *Me*CHCO), 1.48 (6 H, s, Me_2C), 1.38–1.52 and 1.77–1.84 (2 H, 2 m, MeCH_2CH), 2.80–2.90 (1 H, m, *J* 7.0, MeC*H*CO), 2.94 (3 H, s, MeO), 5.70 (1 H, d, *J* 10.1, ArCH=C*H*), 6.11 (1 H, s, C=CHCO), 6.91 (1 H, d, *J* 10.1, ArC*H*=CH) and 7.34–7.42 (5 H, m, arom.); δ_C 11.5 (CH_3, C-18), 15.0 (CH_3, C-19), 24.9 (CH_2, C-6), 28.1 (CH_3, C-16), 28.1 (CH_3, C-17), 48.9 (CH, C-7), 63.8 (MeO), 78.6 (C, C-10), 106.3 (C, C-12a), 106.5 (C, C-4a), 114.1 (CH, C-3), 114.9 (CH, C-12), 122.6 (C, C-8a), 127.4 (CH, C-13), 127.8 (CH, C-14), 128.6 (CH, C-15), 129.5 (CH, C-11), 137.8 (C, C-13a), 150.8 (C, C-12b), 153.1 (C, C-8b), 154.8 (C, C-4), 155.0 (C, C-4b), 159.7 (C, C-2) and 206.2 (C, C-8); *m/z* 418 (M^+, 100%), 403 (14), 386 (1) and 356 (1).

5-Methoxy-8,8-dimethyl-6-(2-methylbutanoyl)-4-propyl-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*']dipyran-2-one 43. This was prepared from 5-hydroxy coumarin **41** (10.66 g, 28.8 mmol) as a yellow oil (10.67 g, 96%), which crystallised on standing, mp 72 °C (Found: M^+, 384.1935. $C_{23}H_{28}O_5$ requires *M*, 384.1937); δ_H 0.95 (3 H, t, *J* 7.4, *Me*CH_2CH), 0.99 (3 H, t, *J* 7.4, *Me*CH_2CH_2), 1.14 (3 H, d, *J* 7.0, *Me*CHCO), 1.35–1.50 and 1.74–1.88 (2 H, 2 m, MeCH_2CH), 1.43 (6 H, s, Me_2C), 1.56–1.68 (2 H, m, MeCH_2CH_2), 2.81 (2 H, m, $MeCH_2CH_2$), 2.78–2.85 (1 H, m, *J* 7.0, MeC*H*CO), 3.73 (3 H, s, MeO), 5.65 (1 H, d, *J* 10.1, ArCH=C*H*), 6.07 (1 H, s, C=CHCO) and 6.83 (1 H, d, *J* 10.1, ArC*H*=CH); δ_C 11.6 (CH_3, C-18), 13.9 (CH_3, C-15), 15.0 (CH_3, C-19), 22.4 (CH_2, C-14), 25.0 (CH_2, C-6), 28.1 (CH_3, C-16), 28.1 (CH_3, C-17), 36.9 (CH_2, C-13), 49.1 (CH, C-7), 65.1 (MeO), 78.4 (C, C-10), 106.4 (C, C-12a), 107.2 (C, C-4a), 112.1 (CH, C-3), 115.1 (CH, C-12), 122.3 (C, C-8a), 129.5 (CH, C-11), 150.6 (C, C-12b), 152.6 (C, C-8b), 155.1 (C, C-4b), 157.0 (C, C-4), 160.1 (C, C-2) and 206.6 (C, C-8); *m/z* 384 (M^+, 23%), 369 (92), 355 (33) and 327 (100).

5,7-Dimethoxy-6-(2-methylbutanoyl)-4-propyl-2*H*-chromen-2-one 60

This was prepared using the procedure above from 5,7-dihydroxy coumarin **33** (1 mol. equiv.) and methyl iodide (4 mol. equiv.) as yellow crystals (83%), mp 73–76 °C (from hexane–dichloromethane); δ_H 0.93 (3 H, t, *J* 7.4, *Me*CH_2CH), 1.00 (3 H, t, *J* 7.3, *Me*CH_2CH_2), 1.13 (3 H, d, *J* 7.0, *Me*CHCO),

1.33–1.48 and 1.72–1.83 (2 H, 2 m, MeCH_2CH), 1.58–1.70 (2 H, m, MeCH_2CH_2), 2.77–2.88 (3 H, 2 m, MeCH_2CH_2 and MeC*H*CO), 3.74 (3 H, s, OMe), 3.83 (3 H, s, OMe), 6.10 (1 H, s, C=CHCO) and 6.66 (1 H, s, arom.); δ_C 11.5 (CH_3, C-4″), 13.9 (CH_3, C-3′), 14.8 (CH_3, C-5″), 22.3 (CH_2, C-2′), 24.9 (CH_2, C-3″), 36.7 (CH_2, C-1′), 49.3 (CH, C-2″), 56.1 (5-MeO), 65.0 (7-MeO), 96.5 (CH, C-8), 107.4 (C, C-10), 112.4 (CH, C-3), 123.1 (C, C-6), 155.7 (C, C-9), 156.7 (C, C-4), 156.7 (C, C-7), 158.9 (C, C-5), 160.4 (C, C-2) and 207.1 (C, C-1″); *m/z* 322 (M^+, 7%), 276 (24), 275 (100), 247 (11) and 217 (8).

5,7-Dimethoxy-6-(1-acetoxy-2-methylbut-1-enyl)-4-propyl-2*H*-chromen-2-one 63

A mixture of 5,7-dimethoxy-6-(2-methylbutanoyl)-4-propyl-2*H*-chromen-2-one **60** (100 mg, 0.31 mmol), isopropenyl acetate (3 cm^3) and TSA (10 mg) were heated at 100 °C for 5 h. The cooled solution was poured into water and extracted with chloroform. The extracts were combined, washed with saturated aqueous sodium hydrogen carbonate, water, and then brine. The solution was dried ($MgSO_4$), and evaporated to leave a yellow oil. Purification on flash column silica gel with pentane–ethyl acetate (8:1 v/v) afforded starting material (51 mg, 51%) followed by a mixture of *cis* and *trans* enol acetates **63** (28 mg, 24%) as a colourless oil; δ_H 1.00 (6 H, t, *J* 7.4, 2 × *Me*CH_2CH_2), 1.01 (3 H, t, *J* 7.4, *Me*CH_2C), 1.09 (3 H, t, *J* 7.5, *Me*CH_2C), 1.59 (3 H, s, MeC=C), 1.56–1.70 (4 H, m, 2 × MeCH_2CH_2), 1.76 (3 H, s, MeC=C), 1.88–2.02 (2 H, m, MeCH_2C), 2.08 (6 H, s, 2 × MeCO), 2.05–2.17 and 2.21–2.36 (2 H, 2 m, MeCH_2C), 2.74–2.94 (4 H, m, 2 × MeCH_2CH_2), 3.78 (3 H, s, OMe), 3.79 (3 H, s, OMe), 3.86 (3 H, s, OMe), 3.87 (3 H, s, OMe), 6.05 (2 H, s, 2 × C=CHCO) and 6.62 (2 H, s, 2 × arom.).

3,4-Dihydro-5-methoxy-2,2-dimethyl-6-(2-methylbutanoyl)-10-propyl-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*′]dipyran-8-one 67

A solution of the pyranocoumarin **38** (0.6 g, 1.5 mmol) in dry ethanol (50 cm^3) containing 10% palladium on carbon catalyst (10 mg) was stirred vigorously under a hydrogen atmosphere. After 1 equiv. of hydrogen had been taken up (in a few seconds), the mixture was filtered through Celite and evaporated. The residue was purified on silica, eluting with dichloromethane to give the pyranocoumarin **67** (0.6 g, 99%) as a colourless gum; δ_H 0.95 (3 H, t, *J* 7.4, *Me*CH_2CH), 1.01 (3 H, t, *J* 7.4, *Me*CH_2CH_2), 1.17 (3 H, d, *J* 7.0, *Me*CHCO), 1.40 (6 H, s, Me_2C), 1.36–1.50 and 1.76–1.90 (2 H, 2 m, MeCH_2CH), 1.55–1.67 (2 H, m, MeCH_2CH_2), 1.81 (2 H, t, *J* 6.7, ArCH_2CH_2), 2.75 (2 H, t, *J* 6.7, ArCH_2CH_2), 2.88 (2 H, m, MeCH_2CH_2), 2.92–3.03 (1 H, m, *J* 6.9, MeC*H*CO), 3.77 (3 H, s, OMe) and 5.98 (1 H, s, C=CHCO); δ_C 11.5 (CH_3, C-18), 13.8 (CH_3, C-15), 14.9 (CH_3, C-19), 17.1 (CH_2, C-8), 23.1 (CH_2, C-14), 25.2 (CH_2, C-10), 26.5 (CH_3, C-16), 26.7 (CH_3, C-17), 31.4 (CH_2, C-7), 38.9 (CH_2, C-13), 49.0 (CH, C-11), 62.4 (MeO), 76.3 (C, C-6), 106.3 (C, C-4a), 110.8 (C, C-8a), 112.6 (CH, C-3), 116.9 (C, C-12a), 151.2 (C, C-12b), 153.5 (C, C-4b), 157.6 (C, C-8b), 157.7 (C, C-4), 159.8 (C, C-2) and 206.2 (C, C-12).

6-(2-Bromo-2-methylbutanoyl)-5-methoxy-2,2-dimethyl-10-propyl-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*′]dipyran-8-one 47

(*a*) Hydrogen bromide gas was passed through a stirred solution of methyl ether **38** (16.4 g, 43 mmol) in dry tetrachloromethane (200 cm^3) at 0 °C. The reaction was monitored by ^{1}H NMR and addition continued (*ca.* 15 min) until the chromene had been completely converted into the HBr adduct **44**, δ_H 0.99 and 1.01 (3 H, 2 t*, *J* 7.4, *Me*CH_2CH), 1.05 (3 H, t, *J* 7.4, *Me*CH_2CH_2), 1.21 and 1.24 (3 H, 2 d*, *J* 7.0, *Me*CHCO), 1.38–1.50 [1 H, 2 m*, MeCH(*H*)CH], 1.50 (3 H, s, MeCO), 1.58–1.71 (2 H, m, MeCH_2CH_2), 1.72 (3 H, s, MeCO), 1.76–1.96 [1 H, 2 m*, MeC*H*(H)CH], 2.48 [1 H, dd, *J* 5.5, 15.6, CH(*H*)CHBr], 2.60 [1 H, dd, *J* 2.9, 15.6, C*H*(H)CHBr], 2.79–3.10 (3 H, 2 m*, MeCH_2CH_2 and MeC*H*CO), 3.94 (3 H, 2 s*, MeO), 5.55 (1 H, dd, *J* 2.9, 5.5, ArC*H*BrCH_2) and 6.06 (1 H, s, C=CHCO). * Indicates signals are twinned due to the presence of a mixture of diastereoisomers.

(*b*) To the above solution under a nitrogen atmosphere, a solution of bromine in dry tetrachloromethane (21 cm^3 of a 2.0 mol dm^{-3} solution) was added dropwise over a period of 5 min. After the addition, the reaction was monitored by ^{1}H NMR until conversion into the dibromo coumarin **45** appeared complete, δ_H 1.05 (3 H, t, *J* 7.3, *Me*CH_2CH), 1.16 and 1.17 (3 H, 2 t*, *J* 7.1, *Me*CH_2CBr), 1.50 (3 H, s, MeCO), 1.59–1.74 (2 H, m, MeCH_2CH_2), 1.73 (3 H, s, MeCO), 1.92 and 1.98 (3 H, s*, MeCBr), 2.03–2.39 (2 H, 2 m*, MeCH_2CBr), 2.49 [1 H, dd, *J* 5.5 and 15.6, CH(*H*)CHBr], 2.61 [1 H, dd, *J* 2.8 and 15.6, C*H*(H)CHBr], 2.78–3.22 (2 H, 2 m*, MeCH_2CH_2), 4.00 and 4.02 (3 H, 2 s*, MeO), 5.54–5.61 (1 H, m, ArC*H*BrCH_2) and 6.04 (1 H, s, C=CHCO). * Indicates signals are twinned due to the presence of a mixture of diastereoisomers.

(*c*) Dry triethylamine (100 cm^3) was carefully added and the solution was stirred overnight. The resultant mixture was partitioned between water and dichloromethane. The organic layer was separated, dried (Na_2SO_4) and evaporated to dryness. Chromatography of the residue on silica (hexane–dichloromethane 1:1 v/v) afforded the *bromoacyl coumarin* **47** (16.0 g, 81%) as a yellow waxy solid, mp 87–90 °C (Found: M^+, 462.1041. $C_{23}H_{27}BrO_5$ requires *M*, 462.1042); δ_H 1.02 (3 H, t, *J* 7.3, *Me*CH_2-CH_2), 1.12 (3 H, t, *J* 7.3, *Me*CH_2CBr), 1.51 (6 H, s, Me_2C), 1.58–1.68 (2 H, m, MeCH_2CH_2), 1.95 (3 H, s, MeCBr), 2.07–2.14 and 2.27–2.34 (2 H, 2 m, MeCH_2CBr), 2.88 (2 H, m, MeCH_2-CH_2), 3.77 (3 H, s, MeO), 5.66 (1 H, d, *J* 10.0, ArCH=C*H*), 6.00 (1 H, s, C=CHCO) and 6.51 (1 H, d, *J* 10.0, ArC*H*=CH); δ_C 10.1 (CH_3, C-18), 13.8 (CH_3, C-15), 22.9 (CH_2, C-14), 27.7 (CH_3, C-16), 27.7 (CH_3, C-17), 28.0 (CH_3, C-19), 35.0 (CH_2, C-10), 38.3 (CH_2, C-13), 63.4 (MeO), 72.1 (C, C-11), 78.1 (C, C-6), 106.2 (C, C-4a), 110.9 (C, C-8a), 112.7 (CH, C-3), 116.2 (C, C-12a), 116.3 (CH, C-8), 128.7 (CH, C-7), 151.1 (C, C-12b), 152.6 (C, C-4b), 154.6 (C, C-8b), 157.1 (C, C-4), 159.0 (C, C-2) and 201.4 (C, C-12); *m/z* 464 (M^+, 27%), 462 (M^+, 30%), 449 (13), 447 (12), 384 (38), 382 (28), 369 (39), 368 (38), 367 (67) and 327 (100).

6-(2-Bromo-2-methylbutanoyl)-5-methoxy-2,2-dimethyl-10-phenyl-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*′]dipyran-8-one 46

This was prepared using the procedure described above from the methyl ether **37** (7.38 g, 17.6 mmol) as white crystals (8.36 g, 95%), mp 132–134 °C (Found: M^+, 496.0888. $C_{26}H_{25}BrO_5$ requires *M*, 496.0885); δ_H 0.97 (6 H, s, Me_2C), 1.18 (3 H, t, *J* 7.3, *Me*CH_2CBr), 2.03 (3 H, s, MeCBr), 2.11–2.23 and 2.31–2.43 (2 H, 2 m, MeCH_2CBr), 3.80 (3 H, s, MeO), 5.50 (1 H, d, *J* 10.0, ArCH=C*H*), 6.05 (1 H, s, C=CHCO), 6.45 (1 H, d, *J* 10.0, ArC*H*=CH), 7.24–7.27 and 7.37–7.41 (5 H, 2 m, arom.); δ_C 10.2 (CH_3, C-18), 26.9 (CH_3, C-16), 26.9 (CH_3, C-17), 28.2 (CH_3, C-19), 35.2 (CH_2, C-10), 63.6 (MeO), 72.3 (C, C-11), 77.6 (C, C-6), 105.7 (C, C-4a), 111.0 (C, C-8a), 114.4 (CH, C-3), 115.9 (CH, C-8), 116.1 (C, C-12a), 127.3 (CH, C-13), 127.5 (CH, C-14), 127.8 (CH, C-15), 129.2 (CH, C-7), 139.4 (C, C-13a), 150.8 (C, C-12b), 152.5 (C, C-4b), 155.0 (C, C-4), 155.3 (C, C-8b), 158.8 (C, C-2) and 201.5 (C, C-12); *m/z* 498 (M^+, 2%), 496 (M^+, 2%), 483 (2), 481 (2), 401 (14) and 361 (100).

6-(2-Bromo-2-methylbutanoyl)-5-methoxy-2,2,10-trimethyl-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*′]dipyran-8-one 48

This was prepared as described above from the methyl ether **39** (10.72 g, 30 mmol) as a gum (9.36 g, 72%) which on standing gave a yellow solid, mp 82–86 °C (Found: M^+, 434.0725. $C_{21}H_{23}BrO_5$ requires *M*, 434.0729); δ_H 1.15 (3 H, t, *J* 7.3, *Me*CH_2CBr), 1.52 and 1.53 (6 H, 2 s, Me_2C), 1.98 (3 H, s, MeCBr), 2.07–2.19 and 2.27–2.39 (2 H, 2 m, MeCH_2CBr), 2.58 (3 H, d, *J* 1.3, *Me*C=CHCO), 3.80 (3 H, s, MeO), 5.67 (1 H, d, *J*

10.0, ArCH=C*H*), 6.02 (1 H, q, *J* 1.3, MeC=C*H*CO) and 6.53 (1 H, d, *J* 10.0, ArC*H*=CH); δ_C 10.2 (CH_3, C-18), 24.4 (CH_3, C-13), 27.7 (CH_3, C-16), 27.8 (CH_3, C-17), 28.1 (CH_3, C-19), 35.1 (CH_2, C-10), 63.6 (MeO), 72.3 (C, C-11), 78.1 (C, C-6), 106.9 (C, C-4a), 111.0 (C, C-8a), 113.4 (CH, C-3), 116.2 (C, C-12a), 116.3 (CH, C-8), 128.9 (CH, C-7), 150.8 (C, C-12b), 153.1 (C, C-4b), 153.4 (C, C-4), 154.7 (C, C-8b), 159.0 (C, C-2) and 201.5 (C, C-12); *m/z* 436 (M^+, 7%), 434 (M^+, 6%), 421 (3), 419 (3), 354 (4), 339 (21) and 299 (100).

6-(2-Bromo-2-methylbutanoyl)-5-methoxy-8,8-dimethyl-4-phenyl-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*']dipyran-2-one 49

This coumarin was prepared as described above (except that chromatography was performed on flash column silica gel with hexane–ethyl acetate as eluent), from the methyl ether **42** (4.17 g, 9.9 mmol) as colourless cubes (2.16 g, 44%), mp 159–161 °C (from hexane–dichloromethane) (Found: M^+, 496.0885. $C_{26}H_{25}BrO_5$ requires *M*, 496.0885); δ_H 1.10 (3 H, t, *J* 7.3, *Me*CH_2CBr), 1.50 (6 H, s, Me_2C), 1.92 (3 H, s, MeCBr), 1.98–2.10 and 2.18–2.32 (2 H, 2 m, MeCH_2CBr), 2.90 (3 H, s, MeO), 5.70 (1 H, d, *J* 10.2, ArCH=C*H*), 6.14 (1 H, s, C=CHCO), 6.91 (1 H, d, *J* 10.2, ArC*H*=CH) and 7.34–7.46 (5 H, m, arom.); δ_C 10.2 (CH_3, C-18), 28.2 (CH_3, C-19), 28.4 (CH_3, C-16), 28.4 (CH_3, C-17), 35.1 (CH_2, C-6), 63.2 (MeO), 71.9 (C, C-7), 79.1 (C, C-10), 106.1 (C, C-4a), 106.3 (C, C-12a), 114.2 (CH, C-3), 114.9 (CH, C-12), 121.3 (C, C-8a), 127.5 (CH, C-14), 128.0 (CH, C-13), 128.9 (CH, C-15), 129.6 (CH, C-11), 137.4 (C, C-13a), 151.0 (C, C-12b), 152.4 (C, C-8b), 154.4 (C, C-4b), 154.5 (C, C-4), 159.8 (C, C-2) and 202.1 (C, C-8); *m/z* 498 (M^+, 6%), 496 (M^+, 6%), 483 (13), 481 (14), 401 (15) and 361 (100).

6-(2-Bromo-2-methylbutanoyl)-5-methoxy-8,8-dimethyl-4-propyl-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*']dipyran-2-one 50

This coumarin was prepared as described above from the methyl ether **43** (14.32 g, 37.3 mmol) as off-white crystals (9.54 g, 55%), mp 93.5–95 °C (Found: M^+, 462.1053. $C_{23}H_{27}BrO_5$ requires *M*, 462.1042); δ_H 0.99 (3 H, t, *J* 7.3, *Me*CH_2CH_2), 1.12 (3 H, t, *J* 7.3, *Me*CH_2CBr), 1.46 (6 H, s, Me_2C), 1.56–1.72 (2 H, m, MeCH_2CH_2), 1.91 (3 H, s, MeCBr), 2.00–2.12 and 2.20–2.33 (2 H, 2 m, MeCH_2CBr), 2.78–2.90 (2 H, m, MeCH$_2$CH_2), 3.69 (3 H, s, MeO), 5.65 (1 H, d, *J* 10.1, ArCH=C*H*), 6.09 (1 H, s, C=CHCO) and 6.84 (1 H, d, *J* 10.1, ArC*H*=CH); δ_C 10.2 (CH_3, C-18), 13.9 (CH_3, C-15), 22.5 (CH_2, C-14), 28.1 (CH_3, C-19), 28.4 (CH_3, C-16), 28.4 (CH_3, C-17), 35.1 (CH_2, C-6), 36.7 (CH_2, C-13), 64.5 (MeO), 71.5 (C, C-7), 78.8 (C, C-10), 106.4 (C, C-12a), 107.0 (C, C-4a), 112.2 (CH, C-3), 115.0 (CH, C-12), 120.9 (C, C-8a), 129.6 (CH, C-11), 152.0 (C, C-8b), 150.7 (C, C-12b), 154.4 (C, C-4b), 156.7 (C, C-4), 160.1 (C, C-2) and 202.2 (C, C-8); *m/z* 464 (M^+, 7%), 462 (M^+, 7%), 449 (15), 447 (16) and 327 (100).

9-Bromo-5-hydroxy-2,2-dimethyl-6-(2-methylbutanoyl)-10-propyl-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*']dipyran-8-one 70

This coumarin was prepared as described above from coumarin **35** (0.66 g, 1.8 mmol) as yellow crystals (300 mg, 38%), mp 123–125 °C; *m/z* (CI +ve) $[M + 1]^+$ 451 and 449; δ_H 0.98 (3 H, t, *J* 7.4, *Me*CH_2CH), 1.12 (3 H, t, *J* 7.3, *Me*CH_2CH_2), 1.24 (3 H, d, *J* 6.7, *Me*CHCO), 1.39–1.51 and 1.84–1.93 (2 H, 2 m, MeCH_2CH), 1.55 (6 H, s, Me_2C), 1.61–1.71 (2 H, m, MeCH_2CH_2), 3.20–3.26 (2 H, m, MeCH$_2$CH_2), 3.78–3.89 (1 H, m, *J* 6.7, MeC*H*CO), 5.60 (1 H, d, *J* 10.1, ArCH=C*H*), 6.73 (1 H, d, *J* 10.1, ArC*H*=CH) and 14.45 (1 H, s, OH); δ_C 11.7 (CH_3, C-18), 14.4 (CH_3, C-15), 16.4 (CH_3, C-19), 21.8 (CH_2, C-14), 27.1 (CH_2, C-10), 28.1 (CH_3, C-16), 28.1 (CH_3, C-17), 38.4 (CH_2, C-13), 47.0 (CH, C-11), 79.9 (C, C-6), 103.2 (C, C-4a), 103.6 (C, C-8a), 106.6 (C, C-12a), 109.0 (C, C-3), 115.9 (CH, C-8), 126.6 (CH, C-7), 155.0 (C, C-12b), 155.4 (C, C-2), 155.8 (C, C-4), 156.2 (C, C-4b), 163.1 (C, C-8b) and 210.4 (C, C-12).

6-Bromo-5,7-dihydroxy-8-(2-methylbutanoyl)-4-propyl-2*H*-chromen-2-one 66

(*a*) To a solution of copper(II) bromide (0.45 g, 2 mmol) in ethyl acetate (1 cm^3) heated to reflux was added coumarin **30** (0.30 g, 1 mmol) in chloroform–ethyl acetate (1/1 v/v; 10 cm^3). The mixture was stirred and heated at reflux for 1.5 h. The cooled solution was filtered, evaporated and purified on silica to afford the 6-*bromo coumarin* **66** (268 mg, 71%) as white needles, mp 173–175 °C (from hexane–chloroform) (Found: M^+, 382.0429. $C_{17}H_{19}O_5Br$ requires *M*, 382.0416); δ_H 0.98 (3 H, t, *J* 7.4, *Me*CH_2CH), 1.03 (3 H, t, *J* 7.3, *Me*CH_2CH_2), 1.26 (3 H, d, *J* 6.7, *Me*CHCO), 1.39–1.53 and 1.82–1.96 (2 H, 2 m, MeCH_2CH), 1.61–1.73 (2 H, m, MeCH_2CH_2), 2.94 (2 H, m, MeCH$_2$CH_2), 3.87–3.98 (1 H, m, *J* 6.7, MeC*H*CO), 6.08 (1 H, s, C=CHCO), 7.03 (1 H, s, OH) and 15.06 (1 H, s, OH); δ_C 11.6 (CH_3, C-4″), 13.9 (CH_3, C-3′), 16.4 (CH_3, C-5″), 22.7 (CH_2, C-2′), 27.1 (CH_2, C-3″), 38.6 (CH_2, C-1′), 47.0 (CH, C-2″), 96.7 (C, C-6), 102.1 (C, C-10), 104.7 (C, C-8), 110.8 (CH, C-3), 155.4 (C, C-4), 156.6 (C, C-9), 158.2 (C, C-5), 158.6 (C, C-2), 163.5 (C, C-7) and 210.5 (C, C-1″); *m/z* 384 (M^+, 9%), 382 (M^+, 9%), 327 (100), 325 (100), 299 (4) and 297 (4).

(*b*) To a stirred solution of coumarin **30** (0.30 g, 1 mmol) in glacial acetic acid (10 cm^3) was added a solution of bromine in glacial acetic acid (1 cm^3 of 1 mol dm^{-3} solution). The mixture was stirred at room temperature until the colour had discharged. The mixture was evaporated under high vacuum to leave a residue. Purification on silica afforded the 6-bromo coumarin **66** (200 mg, 52%), identical with the sample prepared above.

6-(2-Bromo-2-methylbutanoyl)-5,7-dimethoxy-4-propyl-2*H*-chromen-2-one 64

To a stirred solution of coumarin **60** (0.50 g, 1.5 mmol) in dry tetrachloromethane (20 cm^3) was added dropwise a solution of bromine in dry tetrachloromethane (1.5 cm^3 of 1 mol dm^{-3} solution). After the addition was complete the solution was evaporated and the residue was purified by silica column chromatography. Elution with hexane–dichloromethane (3:7 v/v) afforded 3-*bromo*-6-(2-*bromo*-2-*methylbutanoyl*)-5,7-*dimethoxy*-4-*propyl*-2H-*chromen*-2-*one* **65** (120 mg, 16%) as a white solid, mp 150–151 °C; *m/z* (CI +ve) $[M + 1]^+$ 493, 491 and 489; δ_H 1.02 (3 H, t, *J* 7.3, *Me*CH_2CH_2), 1.09 (3 H, t, *J* 7.2, *Me*CH_2CBr), 1.51–1.70 (2 H, m, MeCH_2CH_2), 1.87 (3 H, s, MeCBr), 1.95–2.09 and 2.17–2.31 (2 H, 2 m, MeCH_2CBr) 3.16 (2 H, m, MeCH$_2$CH_2), 3.73 (3 H, s, OMe), 3.85 (3 H, s, MeO) and 6.67 (1 H, arom.); δ_C 10.0 (CH_3, C-4″), 14.2 (CH_3, C-3′), 22.2 (CH_2, C-2′), 27.9 (CH_3, C-5″), 35.0 (CH_2, C-3″), 36.4 (CH_2, C-1′), 56.1 (5-MeO), 64.7 (7-MeO), 71.8 (C, C-2″), 96.4 (CH, C-8), 107.1 (C, C-10), 111.4 (C, C-3), 122.1 (C, C-6), 154.6 (C, C-4), 154.6 (C, C-5), 155.1 (C, C-9), 156.5 (C, C-2), 158.5 (C, C-7) and 201.9 (C, C-1″); followed by the *title compound* **64** (360 mg, 58%) as a colourless gum; *m/z* (CI +ve) $[M + 1]^+$ 413 and 411; δ_H 1.00 (3 H, t, *J* 7.3, *Me*CH_2CH_2), 1.10 (3 H, t, *J* 7.3, *Me*CH_2CBr), 1.57–1.75 (2 H, m, MeCH_2CH_2), 1.88 (3 H, s, MeCBr), 1.98–2.10 and 2.18–2.30 (2 H, 2 m, MeCH_2CBr) 2.60–3.05 (2 H, br m, MeCH$_2$CH_2), 3.73 (3 H, s, OMe), 3.85 (3 H, s, MeO), 6.12 (1 H, s, C=CHCO) and 6.67 (1 H, arom.); δ_C 10.1 (CH_3, C-4″), 13.9 (CH_3, C-3′), 22.4 (CH_2, C-2′), 27.9 (CH_3, C-5″), 34.9 (CH_2, C-3″), 36.5 (CH_2, C-1′), 56.1 (5-MeO), 64.6 (7-MeO), 71.8 (C, C-2″), 96.6 (CH, C-8), 107.4 (C, C-10), 112.5 (CH, C-3), 121.5 (C, C-6), 155.2 (C, C-5), 156.5 (C, C-4), 156.9 (C, C-9), 158.4 (C, C-7), 160.3 (C, C-2) and 202.2 (C, C-1″).

6-(2-Bromo-2-methylbutanoyl)-3,4-dihydro-5-methoxy-2,2-dimethyl-10-propyl-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*']dipyran-8-one 68

Using the procedure described above, the pyranocoumarin **67**

(350 mg, 0.91 mmol) was brominated. Chromatography on silica (hexane–dichloromethane 1:1 v/v) gave 9-*bromo*-6-(2-*bromo*-2-*methylbutanoyl*)-5-*methoxy*-2,2-*dimethyl*-10-*propyl*-3,4-*dihydro*-2H,8H-*benzo*[1,2-b:3,4-b']*dipyran*-8-*one* **69** (50 mg, 10%) as a white solid, mp 107–111 °C; *m/z* (CI +ve) $[M + 1]^+$ 547, 545 and 543; δ_H 1.11 (3 H, t, *J* 7.2, *Me*CH_2CH_2), 1.15 (3 H, t, *J* 7.3, *Me*CH_2CBr), 1.44 (6 H, s, Me_2C), 1.58–1.72 (2 H, m, MeCH_2CH_2), 1.86 (2 H, t, *J* 6.7, ArCH_2CH_2), 1.96 (3 H, s, MeCBr), 2.06–2.19 and 2.25–2.38 (2 H, 2 m, MeCH_2CBr), 2.80 (2 H, m, ArCH_2CH_2), 3.25 (2 H, m, $MeCH_2CH_2$) and 3.80 (3 H, s, MeO); δ_C 10.2 (CH_3, C-18), 14.3 (CH_3, C-15), 17.4 (CH_2, C-8), 21.7 (CH_2, C-14), 26.6 (CH_3, C-16), 26.8 (CH_3, C-17), 28.1 (CH_3, C-19), 31.2 (CH_2, C-7), 35.1 (CH_2, C-10), 38.4 (CH_2, C-13), 62.0 (MeO), 72.4 (C, C-11), 76.8 (C, C-6), 106.4 (C, C-4a), 111.3 (C, C-8a), 111.4 (C, C-3), 115.3 (C, C-12a), 148.7 (C, C-12b), 153.1 (C, C-4b), 155.6 (C, C-2), 155.8 (C, C-4), 157.0 (C, C-8b) and 201.5 (C, C-12); followed by the *title compound* **68** (200 mg, 47%) as a white solid, mp 95–98 °C; *m/z* (CI +ve) $[M + 1]^+$ 467 and 465; δ_H 1.00 (3 H, t, *J* 7.2, *Me*CH_2CH_2), 1.12 (3 H, t, *J* 7.3, *Me*CH_2CBr), 1.40 (6 H, s, Me_2C), 1.55–1.67 (2 H, m, MeCH_2CH_2), 1.81 (2 H, t, *J* 6.8, ArCH_2CH_2), 1.94 (3 H, s, MeCBr), 2.04–2.15 and 2.23–2.35 (2 H, 2 m, MeCH_2CBr), 2.76 (2 H, m, ArCH_2CH_2), 2.87 (2 H, m, $MeCH_2CH_2$), 3.76 (3 H, s, MeO) and 5.97 (1 H, s, C=CHCO); δ_C 10.1 (CH_3, C-18), 13.8 (CH_3, C-15), 17.2 (CH_2, C-8), 23.0 (CH_2, C-14), 26.5 (CH_3, C-16), 26.7 (CH_3, C-17), 27.9 (CH_3, C-19), 31.1 (CH_2, C-7), 34.9 (CH_2, C-10), 39.0 (CH_2, C-13), 61.9 (MeO), 72.2 (C, C-11), 76.4 (C, C-6), 106.1 (C, C-4a), 115.3 (C, C-12a), 112.5 (CH, C-3), 110.7 (C, C-8a), 150.4 (C, C-12b), 153.5 (C, C-4b), 156.8 (C, C-8b), 157.7 (C, C-4), 159.4 (C, C-2) and 201.7 (C, C-12).

Calophyllolide 1

A solution of the bromoacyl coumarin **46** (7.86 g, 15.8 mmol) in dry DBU (25 cm^3) was stirred at room temperature overnight. The resulting mixture was taken up in dichloromethane (150 cm^3), washed with dilute hydrochloric acid, then water and dried (Na_2SO_4). Evaporation left a residue which was purified on a silica column (dichloromethane) to give calophyllolide **1** as pale yellow crystals (3.47 g, 53%), mp 156 °C (from hexane–dichloromethane) (lit.,[2,3] 158 °C, 152–154 °C) (Found: M^+, 416.1627. $C_{26}H_{24}O_5$ requires *M*, 416.1624); δ_H 0.97 (6 H, s, Me_2C), 1.90 (3 H, dd, *J* 1.0, 7.0, *Me*CH=C), 2.01 (3 H, m, MeCCO), 3.75 (3 H, s, MeO), 5.48 (1 H, d, *J* 10.0, ArCH=C*H*), 6.02 (1 H, s, C=CHCO), 6.45 (1 H, d, *J* 10.0, ArC*H*=CH), 6.53–6.61 (1 H, dq, *J* 1.3 and 7.0, MeC*H*=C), 7.23–7.27 and 7.37–7.43 (5 H, 2 m, arom.); δ_C(Table 1); *m/z* 416 (M^+, 31%), 401 (100), 361 (12) and 331 (13).

5-Methoxy-2,2-dimethyl-6-[(*E*)-2-methylbut-2-enoyl]-10-propyl-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*']dipyran-8-one 2

This coumarin was prepared as described above from bromoacyl coumarin **47** (620 mg, 1.34 mmol) as white crystals (230 mg, 71%), mp 123–125 °C (from hexane–dichloromethane) (lit.,[4] 121–123 °C) (Found: M^+, 382.1770. $C_{23}H_{26}O_5$ requires *M*, 382.1780); δ_H 1.03 (3 H, t, *J* 7.3, *Me*CH_2CH_2), 1.51 (6 H, s, Me_2C), 1.58–1.72 (2 H, m, MeCH_2CH_2), 1.85 (3 H, d, *J* 6.9, *Me*CH=C), 1.96 (3 H, s, MeCCO), 2.88 (2 H, m, $MeCH_2CH_2$), 3.74 (3 H, s, MeO), 5.65 (1 H, d, *J* 10.0, ArCH=C*H*), 5.99 (1 H, s, C=CHCO), 6.45–6.52 (1 H, q, *J* 6.9, MeC*H*=C) and 6.54 (1 H, d, *J* 10.0, ArC*H*=CH); δ_C(Table 1); *m/z* 382 (M^+, 53%), 367 (100), 351 (22) and 327 (26).

Oblongulide 51

This coumarin was prepared as described above from the bromoacyl coumarin **48** (9.0 g, 20.7 mmol) as white needles (4.15 g, 57%), mp 83–85 °C (from hexane) (lit.,†††[,5] 126 °C) (Found: M^+, 354.1465. $C_{21}H_{22}O_5$ requires *M*, 354.1467); δ_H 1.52 (6 H, s, Me_2C), 1.86 (3 H, dd, *J* 1.0, 7.0, *Me*CH=C), 1.98 (3 H, m, *Me*CCO), 2.58 (3 H, d, *J* 1.3, *Me*C=CH), 3.75 (3 H, s, MeO), 5.65 (1 H, d, *J* 10.0, ArCH=C*H*), 5.99 (1 H, q, *J* 1.3, MeC=C*H*CO), 6.44–6.53 (1 H, dq, *J* 1.2 and 7.0, MeC*H*=C) and 6.54 (1 H, d, *J* 10.0, ArC*H*=CH); δ_C(Table 1); *m/z* 354 (M^+, 36%), 339 (100), 311 (14) and 299 (16).

5-Methoxy-8,8-dimethyl-6-[(*E*)-2-methylbut-2-enoyl]-4-phenyl-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*']dipyran-2-one 4

This coumarin was prepared as described above (except that purification was performed on flash column silica with hexane–ethyl acetate 4:1 v/v), from the bromoacyl coumarin **49** (820 mg, 1.65 mmol) as colourless needles (247 mg, 36%), mp 168–169 °C (from hexane–dichloromethane) (Found: M^+, 416.1621. $C_{26}H_{24}O_5$ requires *M*, 416.1624); δ_H 1.39 (6 H, s, Me_2C), 1.87 (3 H, d, *J* 7.0, *Me*CH=C), 1.90 (3 H, m, MeCCO), 2.93 (3 H, s, MeO), 5.68 (1 H, d, *J* 10.1, ArCH=C*H*), 6.10 (1 H, s, C=CHCO), 6.46–6.53 (1 H, dq, *J* 1.2, 6.9, MeC*H*=C), 6.91 (1 H, d, *J* 10.1, ArC*H*=CH) and 7.34–7.42 (5 H, m, arom.); δ_C 10.4 (CH_3, C-19), 14.9 (CH_3, C-18), 27.9 (CH_3, C-16), 27.9 (CH_3, C-17), 63.0 (MeO), 78.2 (C, C-10), 106.0 (C, C-12a), 106.3 (C, C-4a), 114.0 (CH, C-3), 115.0 (CH, C-12), 120.4 (C, C-8a), 127.5 (CH, C-13), 127.6 (CH, C-14), 128.4 (CH, C-15), 129.6 (CH, C-11), 138.1 (C, C-13a), 139.5 (C, C-7), 142.8 (CH, C-6), 150.6 (C, C-12b), 153.5 (C, C-8b), 155.0 (C, C-4), 155.0 (C, C-4b), 159.8 (C, C-2) and 194.7 (C, C-8); *m/z* 416 (M^+, 49%) and 401 (100).

5-Methoxy-8,8-dimethyl-6-[(*E*)-2-methylbut-2-enoyl]-4-propyl-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*']dipyran-2-one 55

This coumarin was prepared as described above from the bromoacyl coumarin **50** (9.54 g, 20.6 mmol) as colourless needles (3.88 g, 49%), mp 101–103 °C (from hexane) (Found: M^+, 382.1768. $C_{23}H_{26}O_5$ requires *M*, 382.1780); δ_H 1.00 (3 H, t, *J* 7.3, *Me*CH_2CH_2), 1.36 (6 H, s, Me_2C), 1.57–1.69 (2 H, m, MeCH_2CH_2), 1.87 (3 H, dd, *J* 1.0, 7.0, *Me*CH=C), 1.96 (3 H, m, MeCCO), 2.83 (2 H, m, $MeCH_2CH_2$), 3.72 (3 H, s, MeO), 5.63 (1 H, d, *J* 10.1, ArCH=C*H*), 6.07 (1 H, s, C=CHCO), 6.43–6.52 (1 H, dq, *J* 1.3 and 7.0, MeC*H*=C) and 6.85 (1 H, d, *J* 10.1, ArC*H*=CH); δ_C 10.6 (CH_3, C-19), 14.0 (CH_3, C-15), 15.0 (CH_3, C-18), 22.5 (CH_2, C-14), 28.0 (CH_3, C-16), 28.0 (CH_3, C-17), 37.2 (CH_2, C-13), 63.7 (MeO), 78.1 (C, C-10), 106.0 (C, C-12a), 107.0 (C, C-4a), 111.9 (CH, C-3), 115.2 (CH, C-12), 119.6 (C, C-8a), 129.5 (CH, C-11), 139.7 (C, C-7), 142.8 (CH, C-6), 150.6 (C, C-12b), 153.1 (C, C-8b), 155.3 (C, C-4b), 157.4 (C, C-4), 160.3 (C, C-2) and 195.3 (C, C-8); *m/z* 382 (M^+, 28%), 367 (100) and 339 (7).

5-Methoxy-2,2-dimethyl-6-[(*E*)-2-methylbut-2-enoyl]-10-propyl-3,4-dihydro-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*']dipyran-8-one 71

This coumarin was prepared as described above from the bromoacyl coumarin **68** (180 mg, 0.4 mmol) as a white solid (40 mg, 27%), mp 107–109 °C (from hexane–dichloromethane); *m/z* (CI +ve) $[M + 1]^+$ 385; δ_H 1.02 (3 H, t, *J* 7.4, *Me*CH_2CH_2), 1.40 (6 H, s, Me_2C), 1.56–1.64 (2 H, m, MeCH_2CH_2), 1.81 (2 H, t, *J* 6.7, ArCH_2CH_2), 1.84 (3 H, d, *J* 6.9, *Me*CH=C), 1.97 (3 H, s, MeCCO), 2.73 (2 H, t, *J* 6.7, ArCH_2CH_2), 2.88 (2 H, m, $MeCH_2CH_2$), 3.73 (3 H, s, MeO), 5.96 (1 H, s, C=CHCO) and 6.43–6.50 (1 H, q, *J* 7.0, MeC*H*=C); δ_C 10.7 (CH_3, C-19), 13.9 (CH_3, C-15), 15.1 (CH_3, C-18), 17.3 (CH_2, C-8), 23.2 (CH_2, C-14), 26.6 (CH_3, C-16), 26.6 (CH_3, C-17), 31.4 (CH_2, C-7), 38.9 (CH_2, C-13), 61.4 (MeO), 76.1 (C, C-6), 105.9 (C, C-4a), 110.1

††† In reference 5, we believe the reported melting points for oblongulide and cordatolide A may have been accidentally transposed.

(C, C-8a), 112.4 (CH, C-3), 114.0 (C, C-12a), 140.0 (C, C-11), 143.8 (CH, C-10), 151.4 (C, C-12b), 153.1 (C, C-4b), 157.4 (C, C-8b), 157.8 (C, C-4), 160.2 (C, C-2) and 194.9 (C, C-12).

5-Methoxy-2,2,10-trimethyl-6-[(*Z*)-2-methylbut-2-enoyl]-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*']dipyran-8-one 3

A solution of (*E*)-2-methylbut-2-enoyl coumarin **51** (330 mg, 0.93 mmol) in dry hexane (50 cm^3) was irradiated under a UV lamp (254 nm) for 12 h. The solution was evaporated and the residue was chromatographed on silica (hexane–diethyl ether 3:1 v/v) to afford the angeloyl coumarin **3** as pale yellow crystals (50 mg, 15%), mp 107–111 °C (from hexane) (Found: M^+, 354.1472. $C_{21}H_{22}O_5$ requires *M*, 354.1467); δ_H 1.51 (6 H, s, Me_2C), 1.75–1.80 (3 H, dd, *J* 1.4 and 7.5, *Me*CH=C), 1.95 (3 H, m, MeCCO), 2.58 (3 H, d, *J* 1.2, *Me*C=CHCO), 3.80 (3 H, s, MeO), 5.66 (1 H, d, *J* 10.0, ArCH=C*H*), 6.00 (1 H, q, *J* 1.2, MeC=C*H*CO), 6.14–6.22 (1 H, dq, *J* 1.3, 7.5, MeC*H*=C) and 6.55 (1 H, d, *J* 10.0, ArC*H*=CH); δ_C (Table 1); *m*/*z* 354 (M^+, 38%), 339 (100), 323 (9), 311 (3), 299 (12) and 257 (15); followed by starting material **51** (275 mg, 83%).

5-Hydroxy-2,2-dimethyl-6-[(*E*)-2-methylbut-2-enoyl]-10-phenyl-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*']dipyran-8-one 52

To a stirred solution of calophyllolide **1** (1.60 g, 3.85 mmol) in dry benzene (50 cm^3) under nitrogen was added magnesium iodide–diethyl ether [10 cm^3 of a solution prepared,[55] from magnesium (0.8 g), iodine (4 g), dry diethyl ether (5 cm^3) and dry benzene (10 cm^3), heated to reflux until the solution was colourless], and the mixture was heated at reflux for 2 h. The cooled solution was acidified with dilute hydrochloric acid and extracted with diethyl ether. The combined diethyl ether extracts were washed with water, dried (Na_2SO_4) and evaporated to leave the *5-hydroxy coumarin* **52** as yellow needles (1.50 g, 97%), mp 141–145 °C (from hexane–dichloromethane) (Found: M^+, 402.1468. $C_{25}H_{22}O_5$ requires *M*, 402.1467); δ_H 0.98 (6 H, s, Me_2C), 1.88 (3 H, dd, *J* 1.1 and 7.0, *Me*CH=C), 2.03 (3 H, m, MeCCO), 5.41 (1 H, d, *J* 10.0, ArCH=C*H*), 5.97 (1 H, s, C=CHCO), 6.19–6.27 (1 H, ddq, *J* 1.1, 1.4 and 7.0, MeC*H*=C), 6.62 (1 H, d, *J* 10.0, ArC*H*=CH), 7.23–7.27 and 7.37–7.42 (5 H, 2 m, arom.) and 12.27 (1 H, s, OH); δ_C 13.1 (CH_3, C-19), 14.3 (CH_3, C-18), 27.4 (CH_3, C-16), 27.4 (CH_3, C-17), 78.8 (C, C-6), 102.3 (C, C-4a), 103.8 (C, C-8a), 105.8 (C, C-12a), 112.3 (CH, C-3), 115.3 (CH, C-8), 126.9 (CH, C-7), 127.2 (CH, C-13), 127.5 (CH, C-14), 127.8 (CH, C-15), 134.4 (CH, C-10), 139.3 (C, C-11), 139.8 (C, C-13a), 155.6 (C, C-4b), 155.6 (C, C-12b), 155.7 (C, C-4), 158.9 (C, C-2), 161.2 (C, C-8b) and 200.9 (C, C-12); *m*/*z* 402 (M^+, 28%), 387 (100) and 331 (54).

5-Hydroxy-2,2-dimethyl-6-[(*E*)-2-methylbut-2-enoyl]-10-propyl-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*']dipyran-8-one 53

This coumarin was prepared using the method described above from the 5-methoxy coumarin **2** (1.75 g, 4.6 mmol) as a yellow microcrystalline solid (1.67 g, 99%), mp 137–140 °C (from hexane–dichloromethane) (Found: M^+, 368.1634. $C_{22}H_{24}O_5$ requires *M*, 368.1624); δ_H 1.05 (3 H, t, *J* 7.3, *Me*CH_2CH_2), 1.54 (6 H, s, Me_2C), 1.63–1.70 (2 H, m, MeCH_2CH_2), 1.84 (3 H, dd, *J* 1.1 and 6.9, *Me*CH=C), 1.98 (3 H, s, MeCCO), 2.89 (2 H, m, $MeCH_2CH_2$), 5.59 (1 H, d, *J* 10.0, ArCH=C*H*), 5.96 (1 H, s, C=CHCO), 6.19 (1 H, dq, *J* 1.4 and 6.9, MeC*H*=C), 6.72 (1 H, d, *J* 10.0, ArC*H*=CH) and 12.04 (1 H, s, OH); δ_C 13.0 (CH_3, C-19), 14.0 (CH_3, C-15), 14.3 (CH_3, C-18), 23.2 (CH_2, C-14), 28.2 (CH_3, C-16), 28.2 (CH_3, C-17), 38.8 (CH_2, C-13), 79.4 (C, C-6), 102.9 (C, C-4a), 104.1 (C, C-8a), 105.9 (C, C-12a), 110.9 (CH, C-3), 115.9 (CH, C-8), 126.5 (CH, C-7), 134.5 (CH, C-10), 139.4 (C, C-11), 158.8 (C, C-4b), 156.0 (C, C-12b), 157.9 (C, C-4), 159.2 (C, C-2), 160.3 (C, C-8b) and 200.9 (C, C-12); *m*/*z* 368 (M^+, 22%), 353 (100), 325 (11) and 297 (33).

5-Hydroxy-2,2,10-trimethyl-6-[(*E*)-2-methylbut-2-enoyl]-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*']dipyran-8-one 54

This coumarin was prepared as described above from oblongulide **51** (2.62 g, 7.4 mmol) as a yellow microcrystalline solid (2.50 g, 99%), mp 106–107 °C (from hexane–dichloromethane) (Found: M^+, 340.1310. $C_{20}H_{20}O_5$ requires *M*, 340.1311); δ_H 1.54 (6 H, s, Me_2C), 1.84 (3 H, dd, *J* 1.1, 6.9, *Me*CH=C), 1.97 (3 H, m, MeCCO), 2.57 (3 H, d, *J* 1.2, *Me*C=CHCO), 5.58 (1 H, d, *J* 10.1, ArCH=C*H*), 5.95 (1 H, q, *J* 1.2, MeC=C*H*CO), 6.12–6.20 (1 H, ddq, *J* 1.1, 1.3, 6.9, MeC*H*=C), 6.71 (1 H, d, *J* 10.1, ArC*H*=CH) and 12.07 (1 H, s, OH); δ_C 13.0 (CH_3, C-19), 14.3 (CH_3, C-18), 24.7 (CH_3, C-13), 28.2 (CH_3, C-16), 28.2 (CH_3, C-17), 79.3 (C, C-6), 103.4 (C, C-4a), 103.9 (C, C-8a), 105.9 (C, C-12a), 111.5 (CH, C-3), 115.8 (CH, C-8), 126.7 (CH, C-7), 134.6 (CH, C-10), 139.3 (C, C-11), 154.0 (C, C-4), 155.4 (C, C-4b), 156.4 (C, C-12b), 159.0 (C, C-2), 160.4 (C, C-8b) and 200.8 (C, C-12); *m*/*z* 340 (M^+, 79%), 325 (100), 307 (54), 297 (64) and 285 (48).

Demethylation of 5-methoxy-2,2-dimethyl-6-[(*E*)-2-methylbut-2-enoyl]-10-propyl-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*']dipyran-8-one 2 with boron tribromide

To a stirred solution of tigloyl coumarin **2** (230 mg, 0.6 mmol) in dry dichloromethane (15 cm^3) at −78 °C under a nitrogen atmosphere was added boron tribromide (0.6 cm^3 of 1 mol dm^{-3} solution in dichloromethane). The solution was stirred overnight and allowed to warm to room temperature. The mixture was poured into dilute hydrochloric acid and extracted with dichloromethane. The extracts were combined, dried (Na_2SO_4) and evaporated to leave a residue. Chromatography on silica with hexane–dichloromethane (1:1 v/v) as eluent gave 6-(*3-bromo-2-methylbutanoyl*)-*5-hydroxy-2,2-dimethyl*-10-*propyl*-2H,8H-*benzo*[1,2-b:3,4-b']*dipyran*-*8-one* **72** (70 mg, 30%) as yellow crystals, mp 119–120 °C (from hexane–dichloromethane); *m*/*z* (CI +ve) $[M + 1]^+$ 451 and 449; δ_H 1.06 (3 H, t, *J* 7.3, *Me*CH_2CH_2), 1.38 (3 H, d, *J* 6.9, *Me*CHCO), 1.54 and 1.55 (6 H, 2 s, Me_2C), 1.61–1.73 (2 H, m, MeCH_2CH_2), 1.81 (3 H, d, *J* 6.8, *Me*CHBr), 2.83–2.99 (2 H, m, $MeCH_2CH_2$), 4.23–4.38 (1 H, dq, *J* 6.9 and 9.5, MeC*H*CO), 4.52–4.62 (1 H, dq, *J* 6.8 and 9.5, MeC*H*Br), 5.59 (1 H, d, *J* 10.1, ArCH=C*H*), 6.03 (1 H, s, C=CHCO), 6.74 (1 H, d, *J* 10.1, ArC*H*=CH) and 13.84 (1 H, s, OH); δ_C 14.0 (CH_3, C-15), 16.3 (CH_3, C-19), 23.2 (CH_2, C-14), 23.3 (CH_3, C-18), 28.2 (CH_3, C-16), 28.4 (CH_3, C-17), 39.0 (CH_2, C-13), 50.5 (CH, C-10), 54.4 (CH, C-11), 79.8 (C, C-6), 102.9 (C, C-4a), 104.2 (C, C-8a), 106.0 (C, C-12a), 110.7 (CH, C-3), 115.8 (CH, C-8), 126.4 (CH, C-7), 156.9 (C, C-12b), 156.9 (C, C-4b), 158.4 (C, C-4), 158.9 (C, C-2), 162.6 (C, C-8b) and 207.1 (C, C-12).

5-Hydroxy-8,8-dimethyl-6-[(*E*)-2-methylbut-2-enoyl]-4-phenyl-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*']dipyran-2-one 56

To a stirred solution of the 5-methoxy coumarin **4** (146 mg, 0.35 mmol) in dry dichloromethane (3 cm^3) at −78 °C under nitrogen was added a solution of boron tribromide–dimethyl sulfide complex (351 mm^3 of a 1.0 mol dm^{-3} solution in dichloromethane). The mixture was stirred at −78 °C for 1 h, and then allowed to warm to room temperature with stirring for another 2 h. The solution was poured into water and extracted with dichloromethane. The organic extracts were combined, washed with saturated aqueous sodium hydrogen carbonate, water and dried ($MgSO_4$). Evaporation left an orange residue which was chromatographed on flash column silica (hexane–ethyl acetate 17:3 v/v) to give the *5-hydroxy coumarin* **56** as a yellow oil (21 mg, 15%) (Found: M^+, 402.1465. $C_{25}H_{22}O_5$ requires *M*, 402.1467); δ_H 1.41 (6 H, s, Me_2C), 1.79 (3 H, dd, *J* 1.4, 6.9, *Me*CH=C), 1.90 (3 H, s, MeCCO), 5.59 (1 H, d, *J* 10.1, ArCH=C*H*), 6.00 (1 H, s, C=CHCO), 5.99–6.07 (1 H, dq, *J* 1.4 and 6.9, MeC*H*=C), 6.87 (1 H, d, *J* 10.1, ArC*H*=CH), 7.32–7.43

(5 H, m, arom.) and 11.45 (1 H, s, OH); δ_C 12.5 (CH_3, C-19), 14.0 (CH_3, C-18), 28.3 (CH_3, C-16), 28.3 (CH_3, C-17), 79.0 (C, C-10), 101.8 (C, C-12a), 105.9 (C, C-4a), 107.8 (C, C-8a), 112.7 (CH, C-3), 115.1 (CH, C-12), 126.9 (CH, C-11), 127.2 (CH, C-13), 127.9 (CH, C-14), 128.5 (CH, C-15), 132.7 (CH, C-6), 138.8 (C, C-13a), 139.6 (C, C-7), 155.8 (C, C-12b), 156.7 (C, C-4), 156.7 (C, C-8b), 159.7 (C, C-2), 160.4 (C, C-4b) and 201.5 (C, C-8); *m/z* 402 (M^+, 19%), 387 (100) and 331 (30); followed by starting material **4** (66 mg, 45%).

5-Hydroxy-8,8-dimethyl-6-[(*E*)-2-methylbut-2-enoyl]-4-propyl-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*']dipyran-2-one 57

This coumarin was prepared as described above from the 5-methoxy coumarin **55** (2.24 g, 5.9 mmol) as a white microcrystalline solid (1.05 g, 49%), mp 94.5–98 °C (Found: M^+, 368.1618. $C_{22}H_{24}O_5$ requires *M*, 368.1624); δ_H 1.00 (3 H, t, *J* 7.4, *Me*CH_2CH_2), 1.38 (6 H, s, Me_2C), 1.58–1.71 (2 H, m, MeCH_2CH_2), 1.78 (3 H, dd, *J* 1.1, 7.0, *Me*CH=C), 1.93 (3 H, m, MeCCO), 2.93 (2 H, m, $MeCH_2CH_2$), 5.54 (1 H, d, *J* 10.1, ArCH=C*H*), 5.92–6.00 (1 H, dq, *J* 1.1 and 7.0, MeC*H*=C), 5.96 (1 H, s, C=CHCO), 6.80 (1 H, d, *J* 10.1, ArC*H*=CH) and 12.75 (1 H, s, OH); δ_C 12.7 (CH_3, C-19), 13.9 (CH_3, C-18), 14.0 (CH_3, C-15), 22.7 (CH_2, C-14), 28.3 (CH_3, C-16), 28.3 (CH_3, C-17), 38.3 (CH_2, C-13), 78.9 (C, C-10), 101.6 (C, C-12a), 102.9 (C, C-4a), 107.0 (C, C-8a), 110.3 (CH, C-3), 115.2 (CH, C-12), 126.6 (CH, C-11), 131.3 (CH, C-6), 139.6 (C, C-7), 154.4 (C, C-12b), 156.4 (C, C-8b), 159.1 (C, C-4), 160.1 (C, C-2), 162.1 (C, C-4b) and 202.7 (C, C-8); *m/z* 368 (M^+, 15%), 353 (100), 325 (12), 297 (18) and 269 (7).

(±)-Inophyllum C 7 and (±)-inophyllum E 8

To a stirred solution of the 5-hydroxy coumarin **52** (1.5 g, 3.7 mmol) in dry dichloromethane (5 cm^3) was added dry triethylamine (10 cm^3). The solution was stirred overnight, evaporated to dryness and the residue was chromatographed on a silica column. Elution with hexane–ethyl acetate (9:1 v/v) gave a small amount (25 mg) of a mixture of uncyclised coumarins **76** and **77**. Continued elution with hexane–ethyl acetate (3:1 v/v) afforded (±)-inophyllum C **7** as white crystals (590 mg, 39%), mp 188.5–189.5 °C (from hexane-dichloromethane) (lit.,[2,10] 188 °C, 188–191 °C) (Found: M^+, 402.1470. $C_{25}H_{22}O_5$ requires *M*, 402.1467); δ_H 0.94 and 0.98 (6 H, 2 s, Me_2C), 1.24 (3 H, d, *J* 6.9, MeCHCO), 1.55 (3 H, d, *J* 6.3, MeCHO), 2.52–2.62 (1 H, dq, *J* 6.9, 11.1, MeC*H*CO), 4.28–4.37 (1 H, dq, *J* 6.3 and 11.1, MeC*H*O), 5.42 (1 H, d, *J* 10.0, ArCH=C*H*), 6.04 (1 H, s, C=CHCO), 6.55 (1 H, d, *J* 10.0, ArC*H*=CH), 7.20–7.27 and 7.35–7.40 (5 H, 2 m, arom.); δ_C(Table 1); *m/z* 402 (M^+, 44%), 387 (95), 332 (32), 331 (100) and 303 (18). Further elution with hexane–ethyl acetate (7:3 v/v) afforded (±)-inophyllum E **8** as pale yellow crystals (880 mg, 59%), mp 210–212 °C (from hexane–dichloromethane) (phase change at 148–150 °C) (lit.,[10] 149–151 °C) (Found: M^+, 402.1467. $C_{25}H_{22}O_5$ requires *M*, 402.1467); δ_H 0.95 and 0.98 (6 H, 2 s, Me_2C), 1.18 (3 H, d, *J* 7.2, *Me*CHCO), 1.43 (3 H, d, *J* 6.6, *Me*CHO), 2.66–2.75 (1 H, dq, *J* 3.4 and 7.2, MeC*H*CO), 4.69–4.76 (1 H, dq, *J* 3.4 and 6.5, MeC*H*O), 5.42 (1 H, d, *J* 10.0, ArCH=C*H*), 6.05 (1 H, s, C=CHCO), 6.55 (1 H, d, *J* 10.0, ArC*H*=CH), 7.20–7.24 and 7.36–7.43 (5 H, 2 m, arom.); δ_C (Table 1), *m/z* 402 (M^+, 24%), 387 (85), 322 (20), 331 (100) and 303 (10). The mixture of coumarins **76** and **77** was separated by further chromatography on silica eluting with hexane–dichloromethane (3:2 v/v) to give 5-hydroxy-2,2-dimethyl-6-(2-methylidenebutanoyl)-10-phenyl-2*H*,8*H*-benzo-[1,2-*b*:3,4-*b*']dipyran-8-one **76** as a yellow solid (10 mg, 0.7%), mp 115–116 °C (Found: M^+, 402.1464. $C_{25}H_{22}O_5$ requires *M*, 402.1467); δ_H 0.98 (6 H, s, Me_2C), 1.25 (3 H, t, *J* 7.4, *Me*CH_2), 2.51–2.58 (2 H, dq, *J* 1.4 and 7.4, MeCH_2C), 5.31 [1 H, s, C*H*(H)=CCH_2], 5.42 (1 H, d, *J* 10.1, ArCH=C*H*), 5.42 [1 H, m, CH(*H*)=CCH_2], 5.98 (1 H, s, C=CHCO), 6.63 (1 H, d, *J* 10.1, ArC*H*=CH), 7.23–7.27 and 7.37–7.42 (5 H, 2 m, arom.) and 12.90 (1 H, s, OH); δ_C 12.1 (CH_3, C-18), 25.7 (CH_2, C-10), 27.4 (CH_3, C-16), 27.4 (CH_3, C-17), 79.1 (C, C-6), 102.3 (C, C-4a), 103.5 (C, C-8a), 105.7 (C, C-12a), 112.5 (CH, C-3), 115.1 (CH, C-8), 115.6 (CH_2, C-19), 126.9 (CH, C-7), 127.2 (CH, C-13), 127.5 (CH, C-14), 127.8 (CH, C-15), 139.8 (C, C-13a), 153.0 (C, C-11), 155.4 (C, C-4), 156.3 (C, C-12b), 156.4 (C, C-4b), 158.6 (C, C-2), 162.0 (C, C-8b) and 202.2 (C, C-12); *m/z* 402 (M^+, 65%), 387 (100), 373 (20), 361 (12) and 331 (24); followed by 5-hydroxy-2,2-dimethyl-6-[(*Z*)-2-methylbut-2-enoyl]-10-phenyl-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*']dipyran-8-one **77** as a yellow solid (15 mg, 1%), mp 120–123 °C (Found: M^+, 402.1464. $C_{25}H_{22}O_5$ requires *M*, 402.1467); δ_H 0.98 (6 H, s, Me_2C), 1.62 (3 H, dq, *J* 1.5 and 7.0, *Me*CH=C), 2.09 (3 H, m, *Me*C=CH), 5.42 (1 H, d, *J* 10.1, ArCH=C*H*), 5.59–5.67 (1 H, dq, *J* 1.5 and 7.0, MeC*H*=C), 6.00 (1 H, s, C=CHCO), 6.64 (1 H, d, *J* 10.1, ArC*H*=CH), 7.22–7.27 and 7.37–7.42 (5 H, 2 m, arom.) and 14.10 (1 H, s, OH); δ_C 14.8 (CH_3, C-18), 20.2 (CH_3, C-19), 27.5 (CH_3, C-16), 27.5 (CH_3, C-17), 79.3 (C, C-6), 102.1 (C, C-4a), 103.7 (C, C-8a), 105.6 (C, C-12a), 112.4 (CH, C-3), 115.1 (CH, C-8), 123.7 (CH, C-10), 126.7 (CH, C-7), 127.1 (CH, C-13), 127.5 (CH, C-14), 127.8 (CH, C-15), 138.9 (C, C-11), 139.8 (C, C-13a), 155.5 (C, C-4), 156.7 (C, C-4b), 156.7 (C, C-12b), 158.8 (C, C-2), 163.3 (C, C-8b) and 203.6 (C, C-12); *m/z* 402 (M^+, 26%), 387 (100) and 331 (11).

Cyclisation of 5-hydroxy-2,2-dimethyl-6-[(*E*)-2-methylbut-2-enoyl]-10-propyl-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*']dipyran-8-one 53

Using the above procedure 5-hydroxy coumarin **53** (1.63 g, 4.4 mmol) was cyclised to afford (±)-trans-6,6,10,11-*tetramethyl*-4-*propyl*-2H,6H,12H-10,11-*dihydrobenzo*[1,2-b:3,4-b':5,6b'']*tripyran*-2,12-*dione* **74** as white crystals (780 mg, 48%), mp 172–175 °C (from hexane–dichloromethane) (lit.,[61] 130–132 °C) (Found: M^+, 368.1628. $C_{22}H_{24}O_5$ requires *M*, 368.1624); δ_H 1.02 (3 H, t, *J* 7.3, *Me*CH_2CH_2), 1.21 (3 H, d, *J* 6.9, MeC*H*CO), 1.51 and 1.55 (6 H, 2 s, Me_2C), 1.53 (3 H, d, *J* 6.3, *Me*CHO), 1.57–1.70 (2 H, m, MeCH_2CH_2), 2.49–2.60 (1 H, dq, *J* 6.9, 11.2, MeC*H*CO), 2.85–2.90 (2 H, m, $MeCH_2CH_2$), 4.24–4.34 (1 H, dq, *J* 6.3, 11.2, MeC*H*O), 5.60 (1 H, d, *J* 10.0, ArCH=C*H*), 6.03 (1 H, s, C=CHCO) and 6.64 (1 H, d, *J* 10.0, ArC*H*=CH); δ_C 10.5 (CH_3, C-19), 13.9 (CH_3, C-15), 19.6 (CH_3, C-18), 23.1 (CH_2, C-14), 28.1 (CH_3, C-16), 28.3 (CH_3, C-17), 38.7 (CH_2, C-13), 47.2 (CH, C-11), 79.2 (C, C-6), 79.5 (CH, C-10), 103.5 (C, C-12a), 104.4 (C, C-4a), 105.5 (C, C-8a), 112.0 (CH, C-3), 115.8 (CH, C-8), 127.0 (CH, C-7), 155.5 (C, C-12b), 155.9 (C, C-4b), 157.1 (C, C-4), 159.0 (C, C-8b), 159.7 (C, C-2) and 189.9 (C, C-12); *m/z* 368 (M^+, 32%), 353 (100), 297 (90) and 269 (38); followed by (±)-cis-6,6,10,11-*tetramethyl*-4-*propyl*-2H,6H,12H-10,11-*dihydrobenzo*[1,2-b:3,4-b':5,6-b'']*tripyran*-2,12-*dione* **9** as white crystals (760 mg, 47%), mp 130–132 °C (from hexane–dichloromethane) (lit.,[61] 130–131 °C) (Found: M^+, 368.1625. $C_{22}H_{24}O_5$ requires *M*, 368.1624); δ_H 1.00 (3 H, t, *J* 7.4, *Me*CH_2CH_2), 1.13 (3 H, d, *J* 7.1, *Me*CHCO), 1.39 (3 H, d, *J* 6.6, *Me*CHO), 1.51 and 1.52 (6 H, 2 s, Me_2C), 1.55–1.68 (2 H, m, MeCH_2CH_2), 2.61–2.70 (1 H, dq, *J* 3.3 and 7.1, MeC*H*CO), 2.85 (2 H, m, $MeCH_2CH_2$), 4.65–4.73 (1 H, dq, *J* 3.3 and 6.5, MeC*H*O), 5.58 (1 H, d, *J* 10.0, ArCH=C*H*), 6.01 (1 H, s, C=CHCO) and 6.63 (1 H, d, *J* 10.0, ArC*H*=CH); δ_C (Table 1); *m/z* 368 (M^+, 27%), 353 (100), 297 (78) and 269 (30).

Cyclisation of 5-hydroxy-2,2,10-trimethyl-6-[(*E*)-2-methylbut-2-enoyl]-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*']dipyran-8-one 54

Using the procedure described above the 5-hydroxy coumarin **54** (4.0 g, 11.8 mmol) was cyclised to afford (±)-trans-4,6,6,10,11-*pentamethyl*-2H,6H,12H-10,11-*dihydrobenzo*[1,2-b:3,4-b':5,6-b'']*tripyran*-2,12-*dione* **75** as a white solid (2.05 g, 51%). mp 212–214 °C (Found: M^+, 340.1315. $C_{20}H_{20}O_5$

requires *M*, 340.1311); δ_H 1.21 (3 H, d, *J* 6.9, *Me*CHCO), 1.52 and 1.55 (6 H, 2 s, Me_2C), 1.54 (3 H, d, *J* 6.3, *Me*CHO), 2.49–2.61 (1 H, m, MeC*H*CO), 2.56 (3 H, d, *J* 1.2, *Me*C=CHCO), 4.25–4.35 (1 H, dq, *J* 6.3 and 11.1, MeC*H*O), 5.59 (1 H, d, *J* 10.0, ArCH=C*H*), 6.02 (1 H, q, *J* 1.2, MeC=C*H*CO) and 6.64 (1 H, d, *J* 10.0, ArC*H*=CH); δ_C 10.4 (CH_3, C-19), 19.6 (CH_3, C-18), 24.7 (CH_3, C-13), 27.9 (CH_3, C-16), 28.2 (CH_3, C-17), 47.2 (CH, C-11), 79.1 (C, C-6), 79.5 (CH, C-10), 103.3 (C, C-12a), 104.9 (C, C-4a), 105.5 (C, C-8a), 112.5 (CH, C-3), 115.7 (CH, C-8), 127.1 (CH, C-7), 153.2 (C, C-4), 155.0 (C, C-12b), 156.3 (C, C-4b), 159.1 (C, C-8b), 159.5 (C, C-2) and 189.9 (C, C-12); *m*/*z* 340 (M^+, 80%), 325 (100), 270 (45), 269 (100) and 241 (60); followed by (±)-cis-4,6,6,10,11-*pentamethyl*-2H,6H,12H-10,11-*dihydrobenzo*[1,2-b:3,4-b′:5,6-b″]*tripyran*-2,12-*dione* **73** as white needles (1.80 g, 45%), mp 129–131 °C (from hexane–dichloromethane) (Found: M^+, 340.1310. $C_{20}H_{20}O_5$ requires *M*, 340.1311); δ_H 1.14 (3 H, d, *J* 7.2, *Me*CHCO), 1.41 (3 H, d, *J* 6.6, *Me*CHO), 1.52 and 1.53 (6 H, 2 s, Me_2C), 2.55 (3 H, d, *J* 1.2, *Me*C=CHCO), 2.61–2.69 (1 H, dq, *J* 3.4 and 7.2, MeC*H*CO), 4.66–4.74 (1 H, dq, *J* 3.4 and 6.6, MeC*H*O), 5.59 (1 H, d, *J* 10.0, ArCH=C*H*), 6.02 (1 H, q, *J* 1.2, MeC=C*H*CO) and 6.64 (1 H, d, *J* 10.0, ArC*H*=CH); δ_C 9.2 (CH_3, C-19), 16.0 (CH_3, C-18), 24.7 (CH_3, C-13), 28.1 (CH_3, C-16), 28.2 (CH_3, C-17), 45.9 (CH, C-11), 77.2 (CH, C-10), 79.2 (C, C-6), 102.8 (C, C-12a), 105.0 (C, C-4a), 105.5 (C, C-8a), 112.6 (CH, C-3), 115.7 (CH, C-8), 127.1 (CH, C-7), 153.3 (C, C-4), 155.3 (C, C-12b), 156.5 (C, C-4b), 159.0 (C, C-8b), 159.6 (C, C-2) and 191.6 (C, C-12); *m*/*z* 340 (M^+, 52%), 325 (92), 284 (10), 269 (100) and 241 (33).

(±)-Tomentolide B 81 and (±)-calanolide D 79

Using the procedure described above the 5-hydroxy coumarin **57** (700 mg, 1.9 mmol) was cyclised to afford after chromatography 5-*hydroxy*-8,8-*dimethyl*-6-[(Z)-2-*methylbut*-2-*enoyl*]-4-*propyl*-2H,8H-*benzo*[1,2-b:3,4-b′]*dipyran*-2-*one* **82** (42 mg, 5%) as a yellow solid, mp 114–117 °C (Found: M^+, 368.1621. $C_{22}H_{24}O_5$ requires *M*, 368.1624); δ_H 1.03 (3 H, t, *J* 7.3, *Me*CH_2CH_2), 1.45 (6 H, s, Me_2C), 1.53 (3 H, dd, *J* 1.4 and 7.0, *Me*CH=C), 1.62–1.74 (2 H, m, *J* 7.4, MeCH_2CH_2), 1.97 (3 H, m, MeC=CO), 2.97 (2 H, t, *J* 7.3, $MeCH_2CH_2$), 5.32–5.40 (1 H, dq, *J* 1.4 and 6.9, MeC*H*=C), 5.57 (1 H, d, *J* 10.1, ArCH=C*H*), 5.97 (1 H, s, C=CHCO), 6.80 (1 H, d, *J* 10.1, ArC*H*=CH) and 14.85 (1 H, s, OH); δ_C 14.0 (CH_3, C-15), 14.6 (CH_3, C-18), 20.5 (CH_3, C-19), 22.7 (CH_2, C-14), 27.9 (CH_3, C-16), 27.9 (CH_3, C-17), 38.3 (CH_2, C-13), 79.5 (C, C-10), 101.4 (C, C-12a), 103.0 (C, C-4a), 106.8 (C, C-8a), 110.2 (CH, C-3), 115.2 (CH, C-12), 121.0 (CH, C-6), 126.6 (CH, C-11), 139.8 (C, C-7), 155.7 (C, C-12b), 157.6 (C, C-8b), 159.3 (C, C-4), 159.9 (C, C-2), 164.9 (C, C-4b) and 205.1 (C, C-8); *m*/*z* 368 (M^+, 22%), 353 (100), 327 (21), 325 (9) and 297 (14); followed by starting material **57** (101 mg, 14%), then (±)-tomentolide **B 81** as yellow crystals (100 mg, 14%), mp 154–157 °C (lit.,[6] 158–160 °C) (Found: M^+, 368.1623. $C_{22}H_{24}O_5$ requires *M*, 368.1624); δ_H 1.03 (3 H, t, *J* 7.4, *Me*CH_2CH_2), 1.20 (3 H, d, *J* 6.9, MeC*H*CO), 1.50 and 1.56 (6 H, 2 s, Me_2C), 1.57 (3 H, d, *J* 6.2, *Me*CHO), 1.58–1.71 (2 H, m, MeCH_2CH_2), 2.50–2.61 (1 H, dq, *J* 6.9 and 12.1, MeC*H*CO), 2.89 (2 H, m, $MeCH_2CH_2$), 4.22–4.53 (1 H, dq, *J* 6.2 and 12.1, MeC*H*O), 5.64 (1 H, d, *J* 10.1, ArCH=C*H*), 5.99 (1 H, s, C=CHCO) and 6.81 (1 H, d, *J* 10.1, ArC*H*=CH); δ_C (Table 1); *m*/*z* 368 (M^+, 38%), 353 (100), 298 (17), 297 (80), 269 (18) and 241 (10); followed by (±)-*calanolide D* **79** as yellow crystals (141 mg, 20%), mp 114–117 °C (Found: M^+, 368.1625. $C_{22}H_{24}O_5$ requires *M*, 368.1624); δ_H 1.01 (3 H, t, *J* 7.3, *Me*CH_2CH_2), 1.15 (3 H, d, *J* 7.4, MeC*H*CO), 1.43 (3 H, d, *J* 6.6, *Me*CHO), 1.51 (6 H, s, Me_2C), 1.57–1.69 (2 H, m, MeCH_2CH_2), 2.57–2.66 (1 H, dq, *J* 3.3 and 7.4, MeC*H*CO), 2.78–2.94 (2 H, m, $MeCH_2CH_2$), 4.67–4.74 (1 H, dq, *J* 3.3 and 6.6, MeC*H*O), 5.62 (1 H, d, *J* 10.1, ArCH=C*H*), 5.97 (1 H, s, C=CHCO) and 6.78 (1 H, d, *J* 10.1, ArC*H*=CH); δ_C (Table 1); *m*/*z* 368 (M^+, 32%), 353 (100), 298 (16), 297 (79), 269 (17) and 241 (9).

(±)-Tomentolide A 80 and (±)-*cis* isomer 78

A stirred solution of the 5-hydroxy coumarin **56** (20 mg, 0.05 mmol) in dry triethylamine (2 cm^3) was heated to reflux for 3 h. The cooled solution was evaporated and the residue was chromatographed on flash column silica gel eluting with hexane–ethyl acetate (4:1 v/v) to give (±)-tomentolide A **80** as a pale yellow solid (10 mg, 50%), mp 202–204 °C (lit.,[6] 201–205 °C) (Found: M^+, 402.1471. $C_{25}H_{22}O_5$ requires *M*, 402.1467); δ_H 0.74 (3 H, d, *J* 6.2, *Me*CHO), 1.06 (3 H, d, *J* 6.8, *Me*CHCO), 1.53 and 1.58 (6 H, 2 s, Me_2C), 2.29–2.40 (1 H, dq, *J* 6.8 and 12.4, MeC*H*CO), 3.80–3.90 (1 H, dq, *J* 6.2 and 12.4, MeC*H*O), 5.67 (1 H, d, *J* 10.1, ArCH=C*H*), 6.02 (1 H, s, C=CHCO), 6.86 (1 H, d, *J* 10.1, ArC*H*=CH) and 7.22–7.41 (5 H, m, arom.); δ_C (Table 1); *m*/*z* 402 (M^+, 29%), 387 (100), 332 (18), 331 (89), 303 (8) and 275 (5); followed by (±)-cis-6,7,10,10-*tetramethyl*-4-*phenyl*-2H,6H,12H-6,7-*dihydrobenzo*[1,2-b:3,4-b′:5,6-b″]*tripyran*-2,8-*dione* **78** as a yellow solid (10 mg, 50%), mp 169–171 °C (Found: M^+, 402.1468. $C_{25}H_{22}O_5$ requires *M*, 402.1467); δ_H 0.74 (3 H, d, *J* 6.5, *Me*CHO), 1.00 (3 H, d, *J* 7.2, *Me*CHCO), 1.54 and 1.55 (6 H, 2 s, Me_2C), 2.36–2.44 (1 H, dq, *J* 3.2 and 7.3, MeC*H*CO), 4.20–4.28 (1 H, dq, *J* 3.2 and 6.5, MeC*H*O), 5.67 (1 H, d, *J* 10.1, ArCH=C*H*), 6.02 (1 H, s, C=CHCO), 6.86 (1 H, d, *J* 10.1, ArC*H*=CH) and 7.20–7.42 (5 H, m, arom.); δ_C 9.0 (CH_3, C-19), 15.1 (CH_3, C-18), 28.2 (CH_3, C-16), 28.3 (CH_3, C-17), 45.6 (CH, C-7), 76.5 (CH, C-6), 79.1 (C, C-10), 101.9 (C, C-4a), 103.8 (C, C-12a), 106.5 (C, C-8a), 112.8 (CH, C-3), 114.9 (CH, C-12), 126.8 (CH, C-13), 127.6 (CH, C-14), 128.0 (CH, C-15), 128.1 (CH, C-11), 139.8 (C, C-13a), 154.2 (C, C-12b), 155.7 (C, C-4), 158.2 (C, C-8b), 159.7 (C, C-4b), 159.8 (C, C-2) and 193.0 (C, C-8); *m*/*z* 402 (M^+, 39%), 387 (100), 331 (70) and 303 (7).

(±)-Inophyllum A 24 and (±)-inophyllum D 26

To a stirred solution of potassium hydrogen phthalate (8.8 g, 44 mmol) in methanol (40 cm^3) and water (40 cm^3) at room temperature was added 10% aqueous sodium hydroxide (4.4 cm^3). To this was added (±)-inophyllum E **8** (1.0 g, 2.4 mmol) dissolved in a mixture of methanol (40 cm^3) and THF (40 cm^3). Sodium boranuide (0.88 g, 22 mmol) was added in small portions with vigorous stirring. After the addition, the mixture was stirred for 5 min, then dilute hydrochloric acid was added to it. The mixture was partitioned between water and diethyl ether, the organic layer was separated, washed with water and dried (Na_2SO_4). Evaporation afforded an oil which was chromatographed on silica (hexane–ethyl acetate 4:1 v/v) to afford (±)-inophyllum A **24** as pale yellow crystals (510 mg, 51%), mp 197–198 °C (from hexane–dichloromethane) (lit.,[10,16] 193–195 °C, 200–202 °C) (Found: M^+, 404.1622. $C_{25}H_{24}O_5$ requires *M*, 404.1624); δ_H 0.93 and 0.95 (6 H, 2 s, Me_2C), 1.17 (3 H, d, *J* 7.1, *Me*CHCHOH), 1.43 (3 H, d, *J* 6.8, *Me*CHO), 2.26–2.36 (1 H, ddq, *J* 3.3, 5.0 and 7.1, MeC*H*CHCO), 3.28 (1 H, d, *J* 3.3, CHO*H*), 4.37–4.45 (1 H, dq, *J* 3.3 and 6.8, MeC*H*O), 5.16 (1 H, dd, *J* 3.0 and 5.0, ArC*H*OH), 5.37 (1 H, d, *J* 10.0, ArCH=C*H*), 5.96 (1 H, s, C=CHCO), 6.53 (1 H, d, *J* 10.0, ArC*H*=CH), 7.23–7.26 and 7.37–7.39 (5 H, 2 m, arom.); δ_C (Table 1); *m*/*z* 404 (M^+, 65%), 389 (100), 371 (58) and 333 (94); followed by (±)-*inophyllum D* **26** as a pale yellow oil (10 mg, 1%) (Found: M^+, 404.1619. $C_{25}H_{24}O_5$ requires *M*, 404.1624); δ_H 0.83 (3 H, d, *J* 7.3, *Me*CHCHOH), 0.94 (6 H, s, Me_2C), 1.44 (3 H, d, *J* 6.6, *Me*CHO), 2.02–2.10 (1 H, ddq, *J* 1.9, 2.0 and 7.2, MeC*H*CHCO), 2.95 (1 H, br s, OH), 4.51–4.58 (1 H, dq, *J* 1.9 and 6.6, MeC*H*O), 4.93 (1 H, d, *J* 2.0, ArC*H*OH), 5.37 (1 H, d, *J* 10.0, ArCH=C*H*), 5.98 (1 H, s, C=CHCO), 6.56 (1 H, d, *J* 10.0, ArC*H*=CH) and 7.23–7.43 (5 H, m, arom.); δ_C (Table 1); *m*/*z*

404 (M^+, 35%), 389 (100), 371 (14), 334 (21), 333 (92) and 305 (11); this was followed by starting material **8** (180 mg, 18%).

(±)-Inophyllum B 13 and inophyllum P 18 and soulattrolide 22

These coumarins were prepared as above from sodium boranuide reduction of (±)-inophyllum C **7** (0.44 g, 1.1 mmol). Purification was performed on silica (dichloromethane–methanol 1000:1 v/v) to afford (±)-*inophyllum B* **13** as a pale yellow oil (125 mg, 28%) (Found: M^+, 404.1618. $C_{25}H_{24}O_5$ requires *M*, 404.1624); δ_H 0.91 and 0.97 (6 H, 2 s, Me_2C), 1.18 (3 H, d, *J* 6.8, *Me*CHCHOH), 1.48 (3 H, d, *J* 6.3, *Me*CHO), 1.90–2.02 (1 H, ddq, *J* 6.9, 7.7 and 9.0, MeC*H*CHCO), 3.55 (1 H, d, *J* 3.3, CHO*H*), 3.91–4.01 (1 H, dq, *J* 6.3 and 9.0, MeC*H*O), 4.79 (1 H, dd, *J* 3.1 and 7.7, ArC*H*OH), 5.37 (1 H, d, *J* 10.0, ArCH=C*H*), 5.97 (1 H, s, C=CHCO), 6.61 (1 H, d, *J* 10.0, ArC*H*=CH), 7.23–7.27 and 7.36–7.39 (5 H, 2 m, arom.); δ_C (Table 1); *m/z* 404 (M^+, 27%), 389 (96), 371 (16), 333 (100) and 305 (10); followed by (as a mixture of enantiomers), inophyllum P **18** and soulattrolide **22** as a white solid (125 mg, 28%), mp 197–199 °C (lit.,[15,16] 198–200 °C, 201–202 °C) (Found: M^+, 404.1623. $C_{25}H_{24}O_5$ requires *M*, 404.1624); δ_H 0.94 (6 H, s, Me_2C), 1.17 (3 H, d, *J* 7.0, *Me*CHCHOH), 1.44 (3 H, d, *J* 6.3, *Me*CHO), 1.73–1.85 (1 H, ddq, *J* 3.3, 7.0 and 10.6, MeC*H*CHCO), 2.59 (1 H, br s, OH), 4.24–4.34 (1 H, dq, *J* 6.4 and 10.6, MeC*H*O), 5.04 (1 H, d, *J* 3.3, ArC*H*OH), 5.36 (1 H, d, *J* 10.0, ArCH=C*H*), 5.97 (1 H, s, C=CHCO), 6.54 (1 H, d, *J* 10.0, ArC*H*=CH), 7.22–7.27 and 7.36–7.39 (5 H, 2 m, arom.); δ_C (Table 1); *m/z* 404 (M^+, 22%), 389 (98), 317 (18), 333 (100) and 305 (10); followed by starting material **7** (150 mg, 34%).

Reduction of (±)-*cis*-6,6,10,11-tetramethyl-4-propyl-2*H*,6*H*,-12*H*-10,11-dihydrobenzo[1,2-*b*:3,4-*b*′:5,6-*b*″]tripyran-2,12-dione 9

Using the procedure described above sodium boranuide reduction of (±)-*cis*-2,3-dimethylchromanone **9** (410 mg, 1.1 mmol) afforded after purification on silica (hexane–ethyl acetate 4:1 v/v), (±)-12β-hydroxy-6,6,10β,11β-tetramethyl-4-propyl-2*H*,6*H*,12*H*-10,11-dihydrobenzo[1,2-*b*:3,4-*b*′:5,6-*b*″]-tripyran-2-one **25** as a colourless glass (300 mg, 73%), mp 50–52 °C (lit.,[61] 54–56 °C) (Found: M^+, 370.1787. $C_{22}H_{26}O_5$ requires *M*, 370.1780); δ_H 1.03 (3 H, t, *J* 7.3, *Me*CH_2CH_2), 1.15 (3 H, d, *J* 7.1, *Me*CHCHOH), 1.41 (3 H, d, *J* 6.7, *Me*CHO), 1.49 (6 H, s, Me_2C), 1.60–1.72 (2 H, m, MeCH_2CH_2), 2.23–2.33 (1 H, ddq, *J* 3.4, 5.2 and 7.1, MeC*H*CHCO), 2.80–2.99 (2 H, m, $MeCH_2CH_2$), 3.30 (1 H, br, OH), 4.36–4.43 (1 H, dq, *J* 3.4 and 6.6, MeC*H*O), 5.09 (1 H, d, *J* 5.2, ArC*H*OH), 5.53 (1 H, d, *J* 10.0, ArCH=C*H*), 5.95 (1 H, s, C=CHCO) and 6.63 (1 H, d, *J* 10.0, ArC*H*=CH); δ_C (Table 1); *m/z* 370 (M^+, 24%), 355 (100), 352 (14), 337 (57), 299 (59) and 271 (14); and (±)-12α-*hydroxy*-6,6,10β,11β-*tetramethyl*-4-*propyl*-2H,6H,12H-10,11-*dihydrobenzo*[1,2-b:3,4-b′:5,6-b″]*tripyran*-2-*one* **83** as a pale yellow oil (10 mg, 2%) (Found: M^+, 370.1776. $C_{22}H_{26}O_5$ requires *M*, 370.1780); δ_H 0.80 (3 H, d, *J* 7.3, *Me*CHCHOH), 1.04 (3 H, t, *J* 7.3, *Me*CH_2CH_2), 1.43 (3 H, d, *J* 6.6, *Me*CHO), 1.49 (6 H, s, Me_2C), 1.60–1.72 (2 H, m, MeCH_2CH_2), 1.99–2.07 (1 H, ddq, *J* 1.9, 2.1 and 7.3, MeC*H*CHCO), 2.87–2.92 (2 H, m, $MeCH_2CH_2$), 2.90 (1 H, br s, OH), 4.48–4.55 (1 H, dq, *J* 1.9 and 6.5, MeC*H*O), 4.86 (1 H, d, *J* 2.1, ArC*H*OH), 5.54 (1 H, d, *J* 10.0, ArCH=C*H*), 5.96 (1 H, s, C=CHCO) and 6.66 (1 H, d, *J* 10.0, ArC*H*=CH); δ_C 9.2 (CH_3, C-19), 14.1 (CH_3, C-15), 17.7 (CH_3, C-18), 23.3 (CH_2, C-14), 27.8 (CH_3, C-16), 27.9 (CH_3, C-17), 37.2 (CH, C-11), 38.6 (CH_2, C-13), 64.7 (CH, C-12), 71.2 (CH, C-10), 77.8 (C, C-6), 103.9 (C, C-4a), 104.2 (C, C-12a), 106.1 (C, C-8a), 110.4 (CH, C-3), 116.5 (CH, C-8), 126.9 (CH, C-7), 151.4 (C, C-4b), 153.3 (C, C-8b), 155.1 (C, C-12b), 158.9 (C, C-4) and 161.0 (C, C-2); *m/z* 370 (M^+, 29%), 355 (100), 337 (15), 299 (59) and 271 (13); and starting material **9** (80 mg, 20%).

(±)-Calanolide A 14 and calanolide B 19 and costatolide 23

Using the procedure described above, sodium boranuide reduction of (±)-*trans*-2,3-dimethylchromanone **74** (470 mg, 1.3 mmol) afforded after purification using flash chromatography (dichloromethane–methanol 500:1 v/v) (±)-calanolide A **14** as a pale yellow oil.which eventually afforded white crystals (140 mg, 30%), mp 108–111 °C (lit.,[61] 56–58 °C as ·0.25H_2O) (Found: M^+, 370.1773. $C_{22}H_{26}O_5$ requires *M*, 370.1780); δ_H 1.03 (3 H, t, *J* 7.3, *Me*CH_2CH_2), 1.15 (3 H, d, *J* 6.8, *Me*CHCHOH), 1.46 (3 H, d, *J* 6.4, *Me*CHO), 1.46 and 1.51 (6 H, 2 s, Me_2C), 1.59–1.71 (2 H, m, MeCH_2CH_2), 1.86–1.99 (1 H, ddq, *J* 6.8, 7.5 and 9.0, MeC*H*CHCO), 2.81–2.98 (2 H, m, $MeCH_2CH_2$), 3.60 (1 H, br s, OH), 3.88–3.97 (1 H, dq, *J* 6.4 and 9.0, MeC*H*O), 4.72 (1 H, d, *J* 7.5, ArC*H*OH), 5.54 (1 H, d, *J* 10.0, ArCH=C*H*), 5.94 (1 H, s, C=CHCO) and 6.61 (1 H, d, *J* 10.0, ArC*H*=CH); δ_C (Table 1); *m/z* 370 (M^+, 28%), 355 (100), 337 (15), 299 (48) and 271 (12); and (as a mixture of enantiomers), calanolide B **19** and costatolide **23** as white crystals (130 mg, 28%), mp 172–174 °C (lit.,[18] 181–182 °C) (Found: M^+, 370.1776. $C_{22}H_{26}O_5$ requires *M*, 370.1780); δ_H 1.03 (3 H, t, *J* 7.3, *Me*CH_2CH_2), 1.14 (3 H, d, *J* 7.0, *Me*CHCHOH), 1.43 (3 H, d, *J* 6.3, *Me*CHO), 1.48 and 1.49 (6 H, 2 s, Me_2C), 1.59–1.71 (2 H, m, MeCH_2CH_2), 1.70–1.80 (1 H, ddq, *J* 3.3, 7.0 and 10.7, MeC*H*CHCO), 2.76 (1 H, br s, OH), 2.81–2.97 (2 H, m, $MeCH_2CH_2$), 4.21–4.31 (1 H, dq, *J* 6.3 and 10.7, MeC*H*O), 4.97 (1 H, d, *J* 3.3, ArC*H*OH), 5.53 (1 H, d, *J* 10.0, ArCH=C*H*), 5.94 (1 H, s, C=CHCO) and 6.63 (1 H, d, *J* 10.0, ArC*H*=CH); δ_C (Table 1); *m/z* 370 (M^+, 28%), 355 (100), 337 (14), 299 (45) and 271 (11); and starting material **74** (90 mg, 19%).

(±)-Calanolide C 84

Using the procedure described above, sodium boranuide reduction of (±)-calanolide D **79** (700 mg, 1.9 mmol) afforded after purification on silica (hexane–ethyl acatate 4:1 v/v) (±)-*calanolide C* **84** as white crystals (515 mg, 73%), mp 185.5–188 °C (from hexane–dichloromethane) (Found: M^+, 370.1778. $C_{22}H_{26}O_5$ requires *M*, 370.1780); δ_H 1.00 (3 H, t, *J* 7.3, *Me*CH_2CH_2), 1.08 (3 H, d, *J* 6.9, *Me*CHCHOH), 1.43 (3 H, d, *J* 6.6, *Me*CHO), 1.48 and 1.54 (6 H, 2 s, Me_2C), 1.57–1.68 (2 H, m, MeCH_2CH_2), 2.20–2.30 (1 H, ddq, *J* 2.3, 6.0 and 6.9, MeC*H*CHCO), 2.74–2.96 (2 H, m, $MeCH_2CH_2$), 3.68 (1 H, br s, OH), 4.30 (1 H, dq, *J* 2.3 and 6.6, MeC*H*O), 5.08 (1 H, d, *J* 6.0, ArC*H*OH), 5.59 (1 H, d, *J* 10.1, ArCH=C*H*), 5.96 (1 H, s, C=CHCO) and 6.85 (1 H, d, *J* 10.1, ArC*H*=CH); δ_C (Table 1); *m/z* 370 (M^+, 30%), 355 (100), 337 (17), 299 (66) and 271 (16).

Reduction of (±)-tomentolide B 81

Using the procedure described above, sodium boranuide reduction of tomentolide B **81** (200 mg, 0.54 mmol) afforded after purification by flash chromatography on silica (hexane–ethyl acetate 4:1 v/v), (±)-8β-*hydroxy*-6β,7α,10,10-*tetramethyl*-4-*propyl*-2H,6H,10H-7,8-*dihydrobenzo*[1,2-b:3,4-b′:5,6b″]-*tripyran*-2-*one* **86** as pale yellow crystals (60 mg, 30%), mp 177–180 °C (Found: M^+, 370.1785. $C_{22}H_{26}O_5$ requires *M*, 370.1780); δ_H 1.00 (3 H, t, *J* 7.4, *Me*CH_2CH_2), 1.17 (3 H, d, *J* 6.8, *Me*CHCHOH), 1.47 (3 H, d, *J* 6.3, *Me*CHO), 1.49 and 1.54 (6 H, 2 s, Me_2C), 1.56–1.68 (2 H, m, MeCH_2CH_2), 1.81–1.94 (1 H, ddq, *J* 6.8, 8.8 and 10.0, MeC*H*CHCO), 2.83–2.89 (2 H, m, $MeCH_2CH_2$), 3.77 (1 H, d, *J* 1.8, CHO*H*), 3.86–3.95 (1 H, dq, *J* 6.3 and 10.0, MeC*H*O), 4.61 (1 H, dd, *J* 1.8 and 8.8, ArC*H*OH), 5.59 (1 H, d, *J* 10.1, ArCH=C*H*), 5.97 (1 H, s, C=CHCO) and 6.86 (1 H, d, *J* 10.1, ArC*H*=CH); δ_C 13.9 (CH_3, C-15), 14.5 (CH_3, C-19), 18.6 (CH_3, C-18), 23.0 (CH_2, C-14), 28.2 (CH_3, C-16), 28.3 (CH_3, C-17), 38.7 (CH_2, C-13), 39.9 (CH, C-7), 68.4 (CH, C-8), 74.4 (CH, C-6), 78.9 (C, C-10), 102.9 (C, C-4a), 103.4 (C, C-12a), 110.3 (C, C-8a), 111.1 (CH, C-3), 115.7 (CH, C-12), 126.9 (CH, C-11), 150.5 (C, C-8b), 153.3 (C,

C-4b), 154.1 (C, C-12b), 158.5 (C, C-4) and 160.8 (C, C-2); *m/z* 370 (M^+, 34%), 355 (100), 353 (28), 337 (14) and 299 (52); and (±)-8α-*hydroxy*-6β,7α,10,10-*tetramethy*l-4-*propyl*-2H,6H,10H-7,8-*di-hydrobenzo*[1,2-b:3,4-b′:5,6-b″]*tripyran*-2-*one* **87** as pale yellow crystals (24 mg, 12%), mp 194–196 °C (Found: M^+, 370.1778. $C_{22}H_{26}O_5$ requires *M*, 370.1780); δ_H 1.00 (3 H, t, *J* 7.4, *Me*CH_2CH_2), 1.16 (3 H, d, *J* 7.0, *Me*CHCHOH), 1.45 (3 H, d, *J* 7.3, *Me*CHO), 1.46 and 1.52 (6 H, 2 s, Me_2C), 1.56–1.68 (2 H, m, MeCH_2CH_2), 1.70–1.82 (1 H, ddq, *J* 3.6, 7.1 and 10.6, MeC*H*CHCO), 2.21 (1 H, br s, OH), 2.84–2.89 (2 H, m, $MeCH_2CH_2$), 4.15–4.25 (1 H, dq, *J* 6.3 and 10.6, MeC*H*O), 4.77 (1 H, d, *J* 3.6, ArC*H*OH), 5.58 (1 H, d, *J* 10.1, ArCH=C*H*), 5.93 (1 H, s, C=CHCO) and 6.84 (1 H, d, *J* 10.1, ArC*H*=CH); δ_C 11.9 (CH_3, C-19), 13.9 (CH_3, C-15), 18.6 (CH_3, C-18), 23.1 (CH_2, C-14), 28.1 (CH_3, C-16), 28.4 (CH_3, C-17), 37.8 (CH, C-7), 38.8 (CH_2, C-13), 62.2 (CH, C-8), 73.2 (CH, C-6), 78.3 (C, C-10), 102.4 (C, C-12a), 103.1 (C, C-4a), 110.0 (C, C-8a), 110.7 (CH, C-3), 115.7 (CH, C-12), 127.1 (CH, C-11), 151.0 (C, C-8b), 153.3 (C, C-4b), 154.2 (C, C-12b), 158.7 (C, C-4) and 160.9 (C, C-2); *m/z* 370 (M^+, 31%), 355 (100), 353 (10), 337 (11) and 299 (35); and starting material **81** (45 mg, 23%).

(±)-Cordatolide A 17 and (±)-cordatolide B 21

Using the procedure described above, sodium boranuide reduction of (±)-*trans*-2,3-dimethylchromanone **75** (0.92 g, 2.7 mmol) afforded after purification using flash chromatography (dichloromethane–methanol 250:1 v/v) (±)-cordatolide A **17** as pale yellow crystals (240 mg, 26%), mp 160–162 °C (from hexane–dichloromethane) (lit.,†††[5] 85 °C) (Found: M^+, 342.1468. $C_{20}H_{22}O_5$ requires *M*, 342.1467); δ_H 1.15 (3 H, d, *J* 6.9, *Me*CHCHOH), 1.46 (3 H, d, *J* 6.4, *Me*CHO), 1.46 and 1.51 (6 H, 2 s, Me_2C), 1.87–1.99 (1 H, ddq, *J* 6.9, 7.7 and 9.1, MeC*H*CHCO), 2.57 (3 H, d, *J* 1.2, *Me*C=CHCO), 3.52 (1 H, d, *J* 2.5, CHO*H*), 3.88–3.98 (1 H, dq, *J* 6.5 and 9.1, MeC*H*O), 4.72 (1 H, dd. *J* 2.5 and 7.7, ArC*H*OH), 5.54 (1 H, d, *J* 10.0, ArCH=C*H*), 5.93 (1 H, q, *J* 1.2, MeC=C*H*CO) and 6.61 (1 H, d, *J* 10.0, ArC*H*=CH); δ_C (Table 1); *m/z* 342 (M^+, 30%), 327 (100), 309 (22) and 271 (91); and (±)-cordatolide B **21** as white needles (210 mg, 23%), mp 218–220 °C (from hexane–dichloromethane) (lit.,[5] 178 °C) (Found: M^+, 342.1468. $C_{20}H_{22}O_5$ requires *M*, 342.1467); δ_H 1.14 (3 H, d, *J* 7.1, *Me*CHCHOH), 1.43 (3 H, d, *J* 6.3, *Me*CHO), 1.47 and 1.48 (6 H, 2 s, Me_2C), 1.68–1.82 (1 H, ddq, *J* 3.3. 7.0 and 10.7, MeC*H*CHCO), 2.56 (3 H, d, *J* 1.1, *Me*C=CHCO), 2.60 (1 H, br s, CHO*H*), 4.21–4.31 (1 H, dq, *J* 6.3 and 10.7. MeC*H*O), 4.96 (1 H, d, *J* 3.3, ArC*H*OH), 5.53 (1 H, d, *J* 10.0, ArCH=C*H*), 5.93 (1 H, q, *J* 1.2, MeC=C*H*CO) and 6.62 (1 H, d. *J* 10.0, ArC*H*=CH); δ_C (Table 1); *m/z* 342 (M^+, 26%), 327 (100), 309 (15) and 271 (75); followed by starting material **75** (400 mg, 43%).

(±)-12-Acetoxycalanolide A 15

To a stirred solution of (±)-calanolide A **14** (100 mg, 0.27 mmol) in dry dichloromethane (10 cm^3) and dry pyridine (1 cm^3) at 0 °C was added acetic anhydride (1 cm^3). The solution was stirred overnight, poured into ice–water and the mixture was extracted with dichloromethane. The organic extracts were combined, dried (Na_2SO_4) and evaporated to leave a residue. Purification on a silica column (hexane–ethyl acetate 7:3 v/v) afforded (±)-12-acetoxycalanolide A **15** as white crystals (105 mg, 94%), mp 143 °C (from hexane–dichloromethane) (Found: M^+, 412.1889. $C_{24}H_{28}O_6$ requires *M*, 412.1886); δ_H 1.03 (3 H, t, *J* 7.3, *Me*CH_2CH_2), 1.08 (3 H, d, *J* 7.0, *Me*CHCHOAc), 1.45 (3 H, d, *J* 6.6, *Me*CHO), 1.49 and 1.51 (6 H, 2 s, Me_2C), 1.59–1.72 (2 H, m, MeCH_2CH_2), 2.05–2.17 (1 H, m, MeC*H*CHCOAc), 2.12 (3 H, s, MeCO), 2.81–2.95 (2 H, m, $MeCH_2CH_2$), 4.14–4.23 (1 H, dq, *J* 6.3 and 6.6, MeC*H*O), 5.55 (1 H, d, *J* 10.0, ArCH=C*H*), 5.95 (1 H, s, C=CHCO), 6.00 (1 H, d, *J* 5.5, C*H*OAc) and 6.63 (1 H, d, *J* 10.0, ArC*H*=CH); δ_C (Table 1); *m/z* 412 (M^+, 31%), 397 (100), 369 (19), 353 (36) and 337 (54).

(±)-12α-Acetoxy-6,6,10β,11α-tetramethyl-4-propyl-2*H*,6*H*,12*H*-10,11-dihydrobenzo[1,2-*b*:3,4-*b*′:5,6-*b*″]tripyran-2-one 85

Using the procedure described above, (±)-chromanol **19** (100 mg, 0.27 mmol) was converted into the (±)-*acetoxy coumarin* **85** as white crystals (95 mg, 85%), mp 179–181 °C (Found: M^+, 412.1891. $C_{24}H_{28}O_6$ requires *M*, 412.1886); δ_H 1.02 (3 H, t, *J* 7.4, *Me*CH_2CH_2), 1.03 (3 H, d, *J* 7.0, *Me*CHCHOAc), 1.44 (3 H, d, *J* 6.3, *Me*CHO), 1.48 and 1.50 (6 H, 2 s, Me_2C), 1.58–1.71 (2 H, m, MeCH_2CH_2), 1.86–1.98 (1 H, ddq, *J* 3.5, 7.0 and 10.7, MeC*H*CHCOAc), 2.08 (3 H, s, CH_3CO), 2.79–2.95 (2 H, m, $MeCH_2CH_2$), 4.06–4.16 (1 H, dq, *J* 6.3 and 10.8, MeC*H*O), 5.54 (1 H, d, *J* 10.0, ArCH=C*H*), 5.95 (1 H, s, C=CHCO), 6.40 (1 H, d, *J* 3.5, ArC*H*OAc) and 6.63 (1 H, d, *J* 10.0, ArC*H*=CH); δ_C 11.9 (CH_3, C-19), 13.9 (CH_3, C-15), 18.6 (CH_3, C-18), 20.9 (*Me*CO), 23.1 (CH_2, C-14), 27.7 (CH_3, C-16), 27.9 (CH_3, C-17), 37.8 (CH, C-11), 38.4 (CH_2, C-13), 63.5 (CH, C-12), 73.6 (CH, C-10), 77.8 (C, C-6), 102.3 (C, C-12a), 103.6 (C, C-4a), 105.8 (C, C-8a), 110.9 (CH, C-3), 116.3 (CH, C-8), 126.7 (CH, C-7), 151.8 (C, C-4b), 153.5 (C, C-8b), 154.0 (C, C-12b), 157.7 (C, C-4), 160.0 (C, C-2) and 169.8 (MeCO); *m/z* 412 (M^+, 40%), 397 (100), 369 (18), 353 (77), 337 (73) and 309 (14).

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