Tandem Thermal Claisen–Cope Rearrangements of Coumarate Derivatives. Total Syntheses of the Naturally Occurring Coumarins: Suberosin, Demethylsuberosin, Ostruthin, Balsamiferone and Gravelliferone[1]

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Thermal Claisen rearrangements of derivatives of 4'-*O*-methyl and 4'-*O*-benzyl methyl coumarates **3**, prepared from the corresponding umbelliferone derivatives, have been investigated. Simple allyl derivatives rearrange predominantly to the vacant *ortho*-position while prenyl derivatives undergo a sterically driven tandem *para*-Claisen rearrangement. After thermal rearrangement, the resulting 2'-hydroxycinnamate esters readily relactonise to yield 3-, 6- and 8-allylated coumarin derivatives in synthetically useful yields.

We have recently reported the regioselective Lewis acid catalysed *ortho*-Claisen rearrangement of 4'-allyloxycoumarate esters[2] and have successfully applied this approach to the synthesis of the naturally occurring linear coumarin, demethylsuberosin **1a**, isolated from *Ruta graveolens*.[3] This procedure utilised 7-(1,1-dimethylallyloxy)coumarin, derived originally from the readily available 3-chloro-3-methylbut-1-yne,[4] but it was recognised that extension of this approach to the synthesis of geranyl and farnesyl prenylogues of **1** would necessitate the use of the less readily obtained dehydrolinaloyl or dehydronerolidyl halides. Since the double inversion of a *para*-Claisen rearrangement would permit the use of ethers derived from more readily available prenyl (3-methylbut-2-enyl), geranyl [(*E*)-3,7-dimethylocta-2,6-dienyl] and farnesyl (3,7,11-trimethyldodeca-2,6,10-trienyl) halides, we decided to investigate the application of such an approach to the synthesis of structures **1**.[5]

The 2'-*O*-allyl ethers **4e–f** were readily prepared from 7-methoxycoumarin **2** (R^1 = Me) *via* cleavage to the coumarate ester **3** (R^1 = Me) (NaOMe, MeOH, reflux, 92%) followed by allylation with the requisite bromide **4d**, 96%; **4e**, 91%; **4f**, 89%) (Scheme 1).

Heating these substrates in refluxing diethylaniline for 2 h gave the desired 6-allylated umbelliferone methyl ethers in good yield (**1d**, 80%; **1e**, 80%; **1f**, 78%) with reclosure to the coumarin following the *para*-Claisen rearrangement. This procedure constitutes a direct, efficient synthesis of suberosin, **1d**, a coumarin constituent of the *Pastinaca* species.[6] Accompanying the desired materials were lesser amounts of 3-allylated by-products (**5d**, 12%; **5e**, 14%; **5f**, 14%), the formation of which can be rationalised by initial rearrangement to the 1'-position followed by [3,3]sigmatropic rearrangement to the side chain and relactonisation. Since it was feared that attempted cleavage of the methyl ethers would result in concomitant cyclisation of the acid-sensitive *ortho* side chains,[7] the corresponding benzyl derivatives **4g–i** were prepared *via* the same procedure in high overall yield from 7-benzyloxycoumarin **2** (R^1 = Bz) **4g**, 86%; **4h**, 82%; **4i**, 82%). Rearrangement as before furnished the desired 6-allylated coumarins **1g**, 78%; **1h**, 72%; **1i**,72%), again accompanied by lesser amounts of the 3-allylated coumarins **5g**, 10%; **5h**, 13%; **5i**, 15%). The 6-allyl-7-benzyloxycoumarins were smoothly debenzylated **1g**: BCl_3, CH_2Cl_2 saturated with ethylene, −50 °C; **1h**, i: Raney Ni, H_2, EtOH) to furnish demethylsuberosin **1a**, ostruthin **1b** (isolated from *Pastinaca ostruthium*[8]), and the farnesyl derivative **1c** in 84, 82 and 77% purified yields, respectively.

Table 1

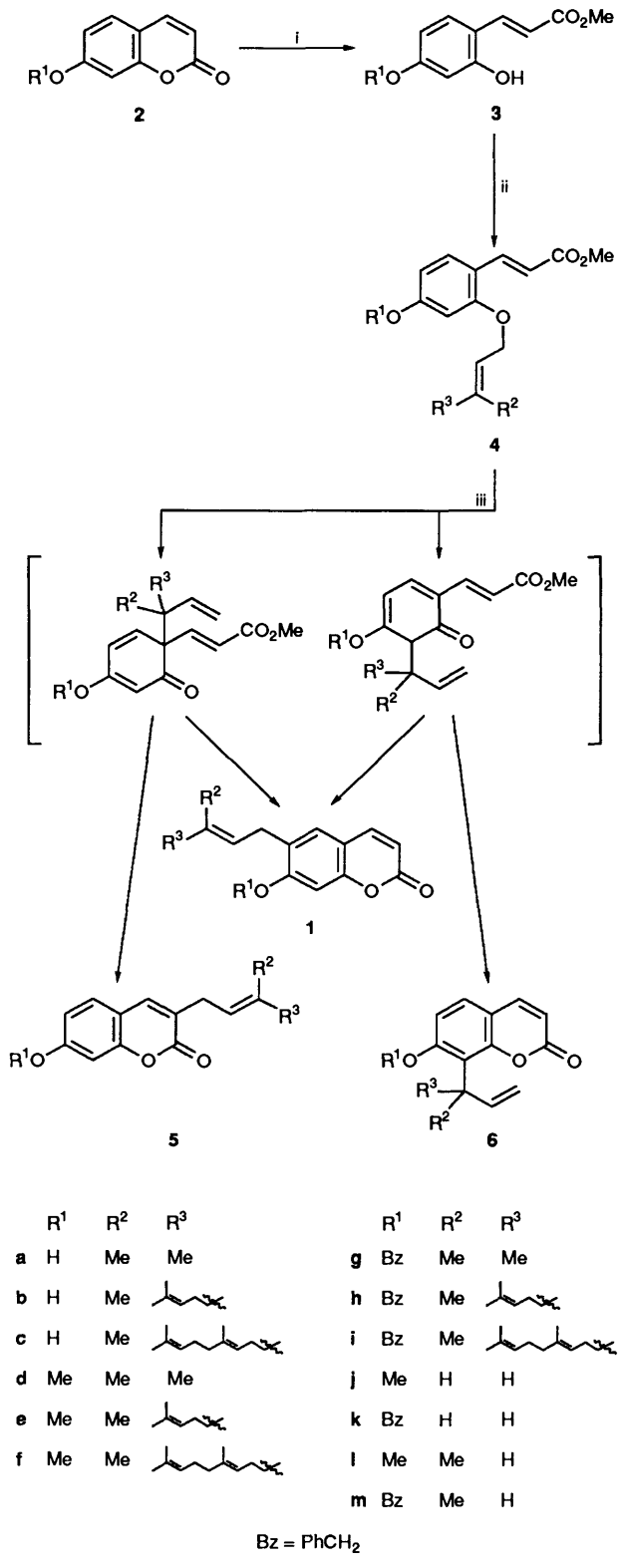
Substrate **4**	Product, isolated yield (%) **1**	**5**	**6**
d	80	12	0
g	78	10	0
j	4	7	84
k	6	8	76
l	28	9	53
m	27	8	50

Examination of the side chain benzylic CH_2 group of the geranyl and farnesyl *para* rearrangement products **1** and **5** by ^1H NMR (300 MHz) in [$^2H_6$]benzene, indicated that the double inversion had predominantly regenerated the initial (2'*E*)-double bond geometry [(*E*):(*Z*) *ca.* 3:1].

The allyl ethers **4j**, **4k** and crotyl (but-2-enyl) ethers **4l**, **4m** were also prepared in order to assess the effect of γ-substitution of the allyl ether upon the *para*-rearrangement process. The allyl ethers furnished largely the 8-substituted umbelliferones **6j** and **6k** (Scheme 1, Table 1), identified by a mutual *ortho* coupling (10 Hz) of the aromatic protons, whereas the crotyl ethers furnished a mixture of 8-(1'-methylallyl)-(**6l**, **6m**) and 6-crotyl-umbelliferones (**1l**, **1m**) (**6**:**1** *ca.* 2:1). These results appear to reflect the degree of steric crowding at the benzylic position of the 8-substituted products.

Interestingly, the yield of 3-substituted umbelliferones **5** produced, appeared insensitive to the nature of the migrating group in all instances. With this alternative rearrangement pathway in mind, syntheses of the naturally occurring 3,6-diprenylated coumarins, balsamiferone **10** (isolated from *Amyris balsamifera*)[9] and gravelliferone **12** (isolated from *R. graveolens*)[10] were undertaken.

The lactone ring of 7-benzyloxy-6-prenylcoumarin **1g** (obtained in 65% yield in four steps from umbelliferone) was cleaved to give the methyl coumarate **7** (NaOMe, MeOH, reflux) and the free phenolic group prenylated (K_2CO_3, prenyl bromide, acetone, reflux) to furnish **8** in 85% overall yield (Scheme 2). On heating in refluxing diethylaniline, **8** smoothly rearranged, resulting in prenyl substitution at the free C-3 position with concomitant relactonisation to produce 7-*O*-benzylbalsamiferone **9** in 95% yield [δ_H(300 MHz; $CDCl_3$) 6.85 (1 H, s, 8-H), 7.17 (1 H, s, 5-H) and 7.32–7.47 (5 H, m, with superimposed s at δ 7.37, benzyl H, 4-H)]. Deprotection (BCl_3,



	R^1	R^2	R^3
a	H	Me	Me
b	H	Me	
c	H	Me	
d	Me	Me	Me
e	Me	Me	
f	Me	Me	

	R^1	R^2	R^3
g	Bz	Me	Me
h	Bz	Me	
i	Bz	Me	
j	Me	H	H
k	Bz	H	H
l	Me	Me	H
m	Bz	Me	H

Scheme 1 *Reagents and conditions:* i, NaOMe, MeOH, reflux; ii, K_2CO_3, $R_2R_3C{=}CHCH_2Br$, acetone, reflux; iii, $PhNEt_2$, reflux

CH_2Cl_2, −50 °C, 90%) furnished the target product **10** [m.p. 134.5–136 °C, lit.,[9] 135–137 °C; δ_H(300 MHz; $CDCl_3$) 6.95 (1 H, s, 8-H) (typical value, 8-H chemical shift concentration dependent) and 7.14 (1 H, s, 5-H)]. This compound has been prepared previously in 13 steps from umbelliferone-3-carboxylic acid in < 1% overall yield.[11] The conversion of **8** into **9** is remarkably efficient in view of the requirement for at least two and possibly four rearrangements.

Gravelliferone **12**, which possesses a 1,1-dimethylallyl substituent at C-3, was prepared by an analogous procedure from demethylsuberosin **1a** (Scheme 3), itself prepared from **1g** in 87% yield. Prenylation of **1a** occurred in 95% yield to give the ether **11** which on heating in refluxing diethylaniline underwent a triple rearrangement to furnish gravelliferone **12** (m.p. 165–166 °C, lit.,[10] 166–168 °C) in 20% purified yield, accompanied by 56% of the starting demethylsuberosin **1a**. In addition, *ca.* 8% of the *ortho*-rearrangement derived product **13** could be isolated from the crude reaction mixture [δ_H(300 MHz; $CDCl_3$) 1.36 (3 H, d, *J* 6 Hz, OCMe), 1.45 (6 H, s, CMe_2), 3.30 (1 H, q, *J* 6 Hz, OCH) and 7.03 (1 H, s, 5-H)].

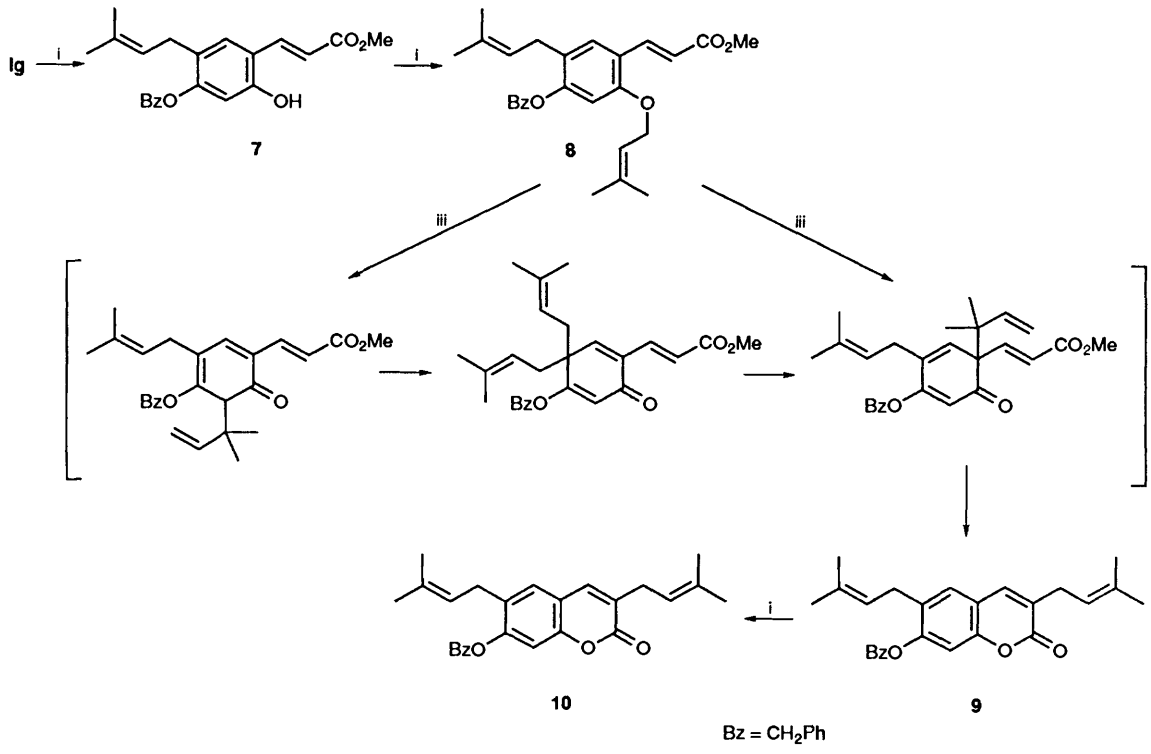
Such a triple rearrangement has been proposed as the biogenetic sequence for the formation of 3-(1,1-dimethylallyl)-umbelliferones[12] and has experimental precedent.[13] Although less efficient than the rearrangement in the balsamiferone series, this migration is still remarkable in view of the sterically unfavourable processes involved. Despite the low yield in the final step, this approach permits the synthesis of gravelliferone in 10% overall yield from umbelliferone which compares favourably with the previous synthesis of this molecule.[14] More recently, Collado *et al.* have utilised an efficient Ireland–Claisen rearrangement of prenyl dihydrocoumarate derivatives as the key step to introduce the 1,1-dimethylallyl side chain onto C-3 of the coumarin nucleus.[15]

The *para*-Claisen rearrangement approach described above permits the ready and efficient preparation of 6-prenylated derivatives of umbelliferone, particularly the higher prenylogues, and is complemented by our *ortho*-Claisen rearrangement approach to 7-allylumbelliferone. In addition balsamiferone **10** and gravelliferone **12** have been prepared in 48% and 10% overall yields, respectively, from umbelliferone, demonstrating further the synthetic utility of multiple [3,3]sigmatropic rearrangements for constructing prenyl substituted coumarins.

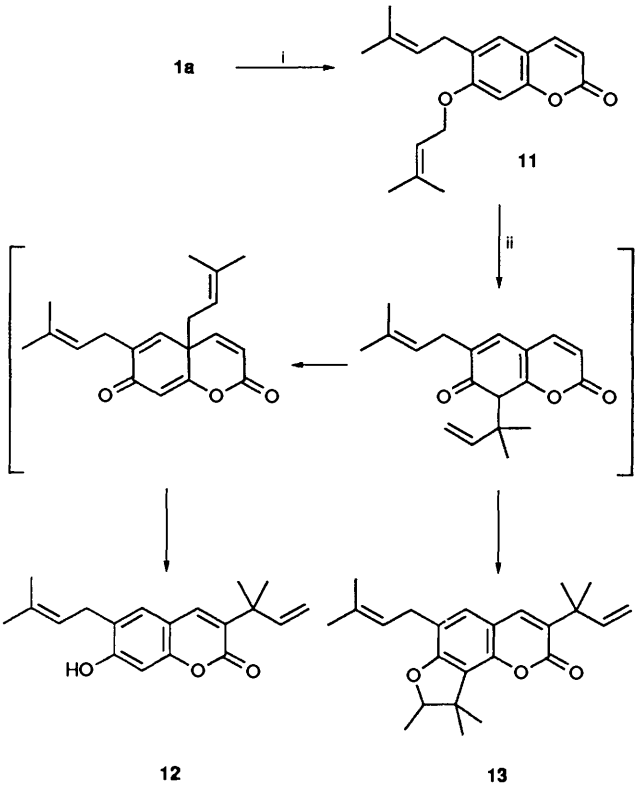
Experimental

General Methods.—Melting points were determined with a Kofler hot stage apparatus and are uncorrected. IR spectra were recorded on Perkin-Elmer 297 and 781 spectrometers. FTIR spectra were recorded on a Perkin-Elmer 1750 spectrometer. UV spectra were recorded on a Perkin-Elmer 555 spectrophotometer. 300 MHz ^1H NMR spectra of solutions in $CDCl_3$, [$^2H_6$]acetone or [$^2H_6$]benzene were recorded on a Bruker WH300 spectrometer. Each signal is described in terms of its chemical shift δ (downfield from tetramethylsilane), integral, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; qn, quintet; m, multiplet) and coupling constant (*J* given in Hz). Mass spectra were recorded on V.G. Micromass 16F and 30F spectrometers. The modes of ionisation used were electron impact (EI), in beam electron impact (IBEI), chemical ionisation (CI) and desorption chemical ionisation (DCI). Ammonia was the ionising source for the chemical ionisation. Flash column chromatography was performed using Kieselgel 60 silica (230–400 mesh, ASTA, 0.04–0.063 nm).[16] TLC was performed using Merck Kieselgel 60 F_{254} plates, which were first observed by UV (254 and 366 nm) and then stained with iodine vapour. Solvents for extractions and chromatography were distilled, otherwise reagent grades were used and all starting materials and reagents were purchased from the Aldrich Chemical Company.

Methyl 2'-Hydroxy-4'-methoxycinnamate **3d**.—7-Methoxycoumarin **2d** (8.00 g, 46 mmol) was added to a freshly prepared solution of sodium methoxide (5.40 g, 100 mmol) in dry methanol (magnesium dried, 300 cm^3) and refluxed for 5 h under nitrogen. The cooled solution was then carefully neutral-



Scheme 2 *Reagents and conditions:* i, NaOMe, MeOH, reflux, 3 h, 92%; ii, prenyl bromide, K_2CO_3, acetone, reflux, 5 h, 95%; iii, $PhNEt_2$, reflux, 3 h, 95%; iv, BCl_3, CH_2Cl_2, −50 °C, 1 h, 90%



Scheme 3 *Reagents and conditions:* i, prenyl bromide, K_2CO_3, acetone, reflux, 5 h, 95%; ii, $PhNEt_2$, reflux, 3 h, **11** 20%, **12** 8%, **1b** 56%

ised with 2 mol dm^{-3} HCl and the resulting precipitate extracted into ethyl ethanoate (100 cm^3), brought to neutrality with brine and then dried over anhydrous magnesium sulfate. Removal of the solvent under reduced pressure afforded methyl 2′-hydroxy-4′-methoxycinnamate **3d** which crystallised as needles from ethyl ethanoate–hexane (8.73 g, 92%), m.p. 144–146.5 °C (Found: C, 63.3; H, 5.9. $C_{11}H_{12}O_4$ requires C, 63.46; H, 5.81%); $\delta_H(CDCl_3)$ 3.80 (3 H, s), 3.82 (3 H, s), 6.42 (1 H, d, *J* 2.5), 6.48 (1 H, dd, *J* 2.5, 8.5), 6.53 (1 H, d, *J* 16), 7.08 (1 H, br s), 7.38 (1 H, d, *J* 8.5) and 7.98 (1 H, d, *J* 16); $\nu_{max}(CHCl_3)/cm^{-1}$ 3590, 1697 and 1612; $\lambda_{max}(CCl_4)/nm$ 292 and 320 ($\log_{10}\varepsilon$ 4.13 and 4.17); *m/z* (IBEI) 208 (M^+, 70%), 176 (71), 148 (100), 133 (51) and 121 (16).

Methyl 4′-Methoxy-2′-(3-methylbut-2-enyloxy)cinnamate **4d**.—Methyl 2′-hydroxy-4′-methoxycinnamate **3d** (5.0 g, 24 mmol) was added to a stirred suspension of anhydrous potassium carbonate (4.14 g, 30 mmol) in acetone (150 cm^3) under nitrogen and then stirred for 30 min. 3-Methylbut-2-enyl bromide (3.7 g, 25 mmol) was added in one portion and the mixture refluxed for 5 h. After filtration and evaporation of the solvent under reduced pressure, the residue was dissolved in ethyl ethanoate (100 cm^3), washed with 2 mol dm^{-3} potassium carbonate (2 × 30 cm^3), then brine to neutrality and dried over anhydrous magnesium sulfate. Flash chromatography (diethyl ether–pentane, 1:9) afforded methyl 4′-methoxy-2′-(3-methylbut-2-enylcinnamate **4d** which crystallised as needles from ethyl ethanoate–hexane, m.p. 46–48 °C (Found: C, 69.2; H, 7.45. $C_{16}H_{20}O_4$ requires C, 69.55; H, 7.30%); $\delta_H(CDCl_3)$ 1.76 (3 H, s), 1.82 (3 H, s), 3.79 (3 H, s), 3.84 (3 H, s), 4.59 (2 H, d, *J* 7.5), 5.52 (1 H, br t, *J* 7.5), 6.43 (1 H, d, *J* 16), 6.45 (1 H, d, *J* 2.5), 6.49 (1 H, dd, *J* 2.5, 8.5), 7.44 (1 H, d, *J* 8.5) and 7.94 (1 H, d, *J* 16); $\nu_{max}(CHCl_3)/cm^{-1}$ 1702, 1627 and 1608; $\lambda_{max}(EtOH)/nm$ 204, 213sh, 240, 291sh, 293 and 327 ($\log_{10}\varepsilon$ 4.23, 4.10, 4.09, 4.09, 4.10 and 4.20); *m/z* (IBEI) 276 (M^+, 5%), 244 (8), 229 (7), 208 (89), 176 (100), 148 (89) and 133 (36).

Thermal Claisen Rearrangement of Methyl 4′-Methoxy-2′-(3-methylbut-2-enyloxy)cinnamate **4d**. *Preparation of Suberosin* **1d**.—Methyl 4′-methoxy-2′-(3-methylbut-2-enyloxy)cinnamate **4d** (1.35 g, 4.89 mmol) was dissolved in diethylaniline (20 cm^3) and the solution refluxed (217 °C) for 4 h under nitrogen when

no starting material was observed by TLC (diethyl ether). After cooling, diethyl ether was added (100 cm^3) to it and the solution washed with 2 mol dm^{-3} hydrochloric acid (5 × 50 cm^3) then with brine to neutrality and dried over anhydrous magnesium sulfate. Removal of the solvent under reduced pressure followed by flash chromatography (diethyl ether–pentane, 1:2) afforded suberosin **1d** [7-methoxy-6-(3-methylbut-2-enyl)coumarin, 0.932 g, 82%] and 7-methoxy-3-(3-methylbut-2-enyl)coumarin **5d** (0.155 g, 14%). **1d** was crystallised from ethyl ethanoate–hexane as needles, m.p. 86.5–88 °C (lit.,[17] 87–88 °C); $\delta_H(CDCl_3)$ 1.71 (3 H, s), 1.79 (3 H, s), 3.31 (2 H, d, *J* 7.5), 3.92 (3 H, s), 5.30 (1 H, br t, *J* 7.5), 6.24 (1 H, d, *J* 9.5), 6.77 (1 H, s), 7.18 (1 H, s) and 7.62 (1 H, d, *J* 16); $\nu_{max}(CHCl_3)/cm^{-1}$ 1732 and 1621; λ_{max}(EtOH)/nm 206, 222, 253, 297 and 330 ($\log_{10}\varepsilon$ 4.35, 4.18, 3.59, 3.79 and 4.07); *m/e* (IBEI) 244 (M^+, 100%), 229 (90) and 189 (12); **5d** was also crystallised from ethyl ethanoate–hexane as needles, m.p. 93.5–95 °C (Found: C, 73.65; H, 6.6. $C_{15}H_{16}O_3$ requires C, 73.75; H, 6.60); $\delta_H(CDCl_3)$ 1.70 (3 H, s), 1.82 (3 H, s), 3.23 (2 H, d, *J* 7.5), 3.87 (3 H, s), 5.31 (1 H, br t, *J* 7.5), 6.83 (2 H, m), 7.31 (1 H, d, *J* 8.5) and 7.39 (1 H, s); $\nu_{max}(CHCl_3)/cm^{-1}$ 1710 and 1614; λ_{max}(EtOH)/nm 206, 212sh, 250, 302 and 319 ($\log_{10}\varepsilon$ 4.12, 4.05, 3.39, 3.93 and 4.11); *m/z* (IBEI) 244 (M^+, 56%), 229 (30), 201 (18) and 189 (100).

Methyl 4′-Benzyloxy-2′-hydroxycinnamate **3g**.—Prepared by the method given above for **3d**. Starting materials: 7-benzyloxycoumarin **2g** (8.32 g, 33 mmol), sodium methoxide solution (10.8 g, 200 mmol of sodium methoxide in 200 cm^3 of magnesium dried methanol), refluxed for 5 h. The product methyl 4-benzyloxy-2′-hydroxycinnamate **3g** (8.44 g, 90%), crystallised from ethyl ethanoate as needles, m.p. 184.5–186 °C (Found: C, 72.1; H, 5.7. $C_{17}H_{16}O_4$ requires C, 71.82; H, 5.67%); $\delta_H(CDCl_3)$ 3.80 (3 H, s), 5.08 (2 H, s), 5.62 (1 H, br s), 6.40 (1 H, d, *J* 2.5), 6.45 (1 H, d, *J* 16), 6.58 (1 H, dd, *J* 2.5, 8.5), 7.37 (6 H, m) and 7.87 (1 H, d, *J* 16); ν_{max}(Nujol mull)/cm^{-1} 3310, 1690, 1626, 1600 and 1583; λ_{max}(EtOH)/nm 204, 240, 291sh and 328 ($\log_{10}\varepsilon$ 4.23, 3.83, 4.02, 4.03 and 4.13); *m/z* (IBEI) 284 (M^+, 9%) and 91 (100).

Methyl 4′-Benzyloxy-2′-(3-methylbut-2-enyloxy)cinnamate **4g**.—Prepared by the method given above for **4d**. Starting materials: methyl 4′-benzyloxy-2′-hydroxycinnamate **3g** (0.50 g, 1.76 mmol), potassium carbonate (1.38 g, 10 mmol), 3-methylbut-2-enyl bromide (0.50 g, 3.0 mmol), acetone (50 cm^3), refluxed for 5 h. Flash chromatography (diethyl ether–pentane, 1:9) afforded methyl 4′-benzyloxy-2′-(3-methylbut-2-enyloxy)-cinnamate **4g** (0.58 g, 94%) which crystallised from diethyl ether–pentane as needles, m.p. 59–61 °C (Found: C, 75.1; H, 6.95. $C_{22}H_{24}O_4$ requires C, 74.98; H, 6.86%); $\delta_H(CDCl_3)$ 1.74 (3 H, s), 1.81 (3 H, s), 3.79 (3 H, s), 4.55 (2 H, d, *J* 7.5), 5.08 (2 H, s), 5.50 (1 H, m), 6.43 (1 H, d, *J* 16), 6.55 (2 H, m), 7.38 (6 H, m) and 7.92 (1 H, d, *J* 16); $\nu_{max}(CHCl_3)/cm^{-1}$ 1701, 1614 and 1605; λ_{max}(EtOH)/nm 203, 240, 293 and 326 ($\log_{10}\varepsilon$ 4.42, 4.04, 4.07 and 4.18); *m/z* (IBEI) 352 (M^+, 1%), 284 (9) and 91 (100).

Thermal Claisen Rearrangement of Methyl 4′-Benzyloxy-2′-(3-methylbut-2-enyloxy)cinnamate **4g**.—Performed by the method given above for **1d**. Starting materials: methyl 4′-benzyloxy-2′-(3-methylbut-2-enyloxy)cinnamate **4g** (0.90 g, 2.56 mmol), diethylaniline (20 cm^3), refluxed for 3 h. Flash chromatography (diethyl ether–pentane, 1:4) afforded 7-benzyloxy-6-(3-methylbut-2-enyl)coumarin **1g** (0.64 g, 78%) and 7-benzyloxy-3-(3-methylbut-2-enyl)coumarin **5g** (0.081 g, 10%). **1g** was crystallised from ethyl ethanoate–hexane as needles, m.p. 104–104.5 °C (Found: C, 78.6; H, 6.3. $C_{21}H_{20}O_3$ requires C, 78.73; H, 6.29%); $\delta_H(CDCl_3)$ 1.67 (3 H, s), 1.78 (3 H, s), 3.38 (2 H, d, *J* 7.5), 5.15 (2 H, s), 5.30 (1 H, m), 6.23 (1 H, d, *J* 9.5), 6.83 (1 H, s), 7.20 (1 H, s), 7.38 (5 H, m) and 7.62 (1 H, d, *J* 9.5); $\nu_{max}(CHCl_3$, FTIR)/cm^{-1} 1719 and 1620; λ_{max}(EtOH)/nm 206, 220sh, 252, 298 and 329 ($\log_{10}\varepsilon$ 4.26, 4.11, 3.52, 3.74 and 4.00); *m/z* (IBEI) 320 (M^+, 12%), 229 (16) and 91 (100). **5g** was also crystallised from ethyl ethanoate–hexane as needles, m.p. 105–106 °C (Found: C, 78.65; H, 6.4. $C_{21}H_{20}O_3$ requires C, 78.73; H, 6.29%); $\delta_H(CDCl_3)$ 1.71 (3 H, s), 1.83 (3 H, s), 3.23 (2 H, d, *J* 7.5), 5.13 (2 H, s), 5.32 (1 H, m), 6.90 (2 H, m) and 7.35 (7 H, m); $\nu_{max}(CHCl_3$, FTIR)/cm^{-1} 1709 and 1615; λ_{max}(EtOH)/nm 207, 250, 290sh, 298sh and 320 ($\log_{10}\varepsilon$ 4.35, 3.53, 3.93, 4.03 and 4.22); *m/z* (EI) 320 (M^+, 18%) and 91 (100).

Demethylsuberosin **1a**.—Boron trichloride (0.07 g, 0.60 mmol, 0.60 cm^3 of a 1 mol dm^{-3} solution in dichloromethane) was added dropwise over 5 min to a stirred solution of 7-benzyloxy-6-(3-methylbut-2-enyl)coumarin **1g** (0.1 g, 0.3 mmol), at −50 °C in dichloromethane (10 cm^3) under nitrogen and left to stand for 1 h. The mixture was then quenched at −50 °C with methanol (5 cm^3), poured into ice–water, extracted with ethyl ethanoate (2 × 20 cm^3), washed with saturated sodium hydrogen carbonate (3 × 15 cm^3), brought to neutrality with brine and then dried over anhydrous magnesium sulfate. Removal of the solvent under reduced pressure followed by flash chromatography (diethyl ether–pentane, 1:4) afforded demethylsuberosin **1a** (0.074 g, 84%) which crystallised from ethyl ethanoate–hexane as needles, m.p. 133–135 °C (lit.,[4] 133.5–134 °C); $\delta_H(CDCl_3)$ 1.78 (3 H, s), 1.80 (3 H, s), 3.37 (2 H, d, *J* 7.5), 5.33 (1 H, br t, *J* 7.5), 6.23 (1 H, d, *J* 9.5), 6.60 (1 H, br s), 6.92 (1 H, s), 7.20 (1 H, s) and 7.63 (1 H, d, *J* 9.5); $\nu_{max}(CHCl_3)/cm^{-1}$ 3580. 1722 and 1628; λ_{max}(EtOH)/nm 204, 212sh, 277 and 319 ($\log_{10}\varepsilon$ 4.23, 4.08, 3.76 and 3.62); *m/z* (NH_3, CI) 231 ($M^+ + 1$, 100%) and 175 (8).

Methyl (E)-*4′-Benzyloxy-2′-(3,7-dimethylocta-2,6-dienyloxy)-cinnamate* **4h**.—Prepared by the method given above for methyl **4d**. Starting materials: 4′-benzyloxy-2′-hydroxycinnamate **3g** (2.0 g, 7.04 mmol), potassium carbonate (2.76 g, 20 mmol), 3,7-dimethylocta-2,6-dienyl bromide (1.53 g, 7.04 mmol), acetone (100 cm^3), refluxed for 8 h. Flash chromatography (diethyl ether–pentane, 1:9) afforded methyl 4′-benzyloxy-2′-(3,7-dimethylocta-2,6-dienyloxy)cinnamate **4h** (2.70 g, 91%) as a colourless oil (Found: C, 77.1; H, 7.65. $C_{27}H_{32}O_4$ requires C, 76.99; H, 7.67%); $\delta_H(CDCl_3)$ 1.64 (3 H, s), 1.71 (3 H, s), 1.75 (3 H, s), 2.15 (4 H, m), 3.79 (3 H, s), 4.58 (2 H, d, *J* 7.5), 5.08 (2 H, s), 5.12 (1 H, m), 5.53 (1 H, m), 6.47 (1 H, d, *J* 16), 6.65 (2 H, m), 7.41 (6 H, m) and 7.97 (1 H, d, *J* 16); $\nu_{max}(CHCl_3)/cm^{-1}$ 1702, 1605, 1570 and 1503; λ_{max}(EtOH)/nm 202, 238, 288sh, 293sh and 324 ($\log_{10}\varepsilon$ 4.00, 3.34, 3.30, 3.31 and 3.42); *m/z* (NH_3, DCI) 421 ($M^+ + 1$, 75%), 302 (18), 285 (100), 253 (14), 195 (17) and 137 (63).

Thermal Claisen Rearrangement of Methyl (E)-*4′-Benzyloxy-2′-(3,7-dimethylocta-2,6-dienyloxy)cinnamate* **4h**.—Performed by the method given above for **1d**. Starting materials: methyl 4′-benzyloxy-2′-(3,7-dimethylocta-2,6-dienyloxy)cinnamate **4h** (1.00 g, 2.38 mmol), diethylaniline (20 cm^3), refluxed for 5 h. The products were not isolated at this stage; the mixture was debenzylated (next experiment) and then separated by HPLC. [However, the product ratio by GC and 500 MHz ^1H NMR = 6:2:1 for 7-benzyloxy-6-(3,7-dimethylocta-2,6-dienyl)coumarin **1h**: 7-benzyloxy-8-(3,7-dimethylocta-1,6-dien-3-yl)coumarin **6h**: 7-benzyloxy-3-(3,7-dimethylocta-2,6-dienyl)coumarin **6h**, respectively.]

Ostruthin (E)-(3,7-*Dimethylocta-2,6-dienyl*)-7-*hydroxycoumarin*) **1b**.—The mixture obtained from the previous experiment was partially separated by flash chromatography (diethyl ether–pentane, 1:8) into 3-substituted and 6-substituted isomers, the former were not investigated further. The latter mixture (0.10 g, 0.26 mmol) was dissolved in absolute ethanol

(15 cm^3) and hydrogenated at ambient temperature and pressure using a Raney nickel catalyst (0.01 g) until 1 mol equiv. of hydrogen had been taken up. After filtration and removal of the solvent (**CARE!**) the residue was subjected to purification by HPLC (Spherisorb cyano column, 5 micron particle size, 25 cm × 2 cm internal diameter, ethyl ethanoate–hexane, 1:12 17 cm^3 min^{-1} 254 nm detector). This afforded ostruthin **1b** (0.059 g, 77%) which crystallised from chloroform–hexane as plates, m.p. 114–116 °C (lit.,[18] 117–119 °C); $\delta_H(CDCl_3)$ 1.60 (3 H, s), 1.68 (3 H, s), 1.72 (3 H, s), 2.10 (4 H, m), 3.36 (2 H, d, *J* 7.5), 5.10 (1 H, m), 5.32 (1 H, m), 6.22 (1 H, d, *J* 9.5), 7.06 (1 H, s), 7.18 (1 H, s) and 7.65 (1 H, d, *J* 9.5); $\nu_{max}(CHCl_3$, FTIR)/cm^{-1} 3290, 1698 and 1621; λ_{max}(EtOH)/nm 209, 220sh, 247, 256, 308 and 335 ($\log_{10}\varepsilon$ 4.61, 4.49, 4.04, 3.99, 4.14 and 4.41); *m/z* (CH_4, CI) 299 ($M^+ + 1$, 100%) and 175 (11).

Methyl 2'-Allyloxy-4'-methoxycinnamate **4j**.—Prepared by the method given above for **4d**. Starting materials: methyl 2'-hydroxy-4'-methoxycinnamate **3d** (1.0 g, 4.27 mmol), potassium carbonate (2.76 g, 20 mmol), allyl bromide (1.21 g, 10 mmol), acetone (50 cm^3), refluxed for 5 h. The product, methyl 2'-allyloxy-4'-methoxycinnamate **4j** (0.996 g, 94%), was crystallised from ethyl ethanoate–hexane as needles, m.p. 51.5–53 °C (Found: C, 67.9; H, 6.6. $C_{14}H_{16}O_4$ requires C, 67.73; H, 6.50%); $\delta_H(CDCl_3)$ 3.80 (3 H, s), 3.83 (3 H, s), 4.61 (2 H, d, *J* 6), 5.32 (1 H, dd, *J* 1.5, 10), 5.43 (1 H, dd, *J* 1.5, 17), 6.08 (1 H, m), 6.43 (1 H, d, *J* 16), 6.44 (1 H, d, *J* 2.5), 6.52 (1 H, dd, *J* 2.5, 8.5), 7.45 (1 H, d, *J* 8.5) and 7.95 (1 H, d, *J* 16); $\nu_{max}(CHCl_3)$/cm^{-1} 1702, 1626 and 1606; λ_{max}(EtOH)/nm 203, 215, 239, 293 and 324 ($\log_{10}\varepsilon$ 4.16, 4.13, 4.14, 4.20 and 4.30); *m/z* (EI) 248 (M^+, 100%), 217 (38), 207 (22), 189 (25), 175 (57), 159 (36), 148 (92), 133 (69) and 99 (44).

Thermal Claisen Rearrangement of Methyl 2'-Allyloxy-4'-methoxycinnamate **4j**.—Performed by the method given above for **1d**. Starting materials: methyl 2'-allyloxy-4'-methoxycinnamate **4j** (0.99 g, 3.99 mmol), diethylaniline (20 cm^3), refluxed for 4 h. Flash chromatography (diethyl ether–pentane, 1:4) afforded 8-allyl-7-methoxycoumarin **6j** (0.72 g, 84%), 6-allyl-7-methoxycoumarin **1j** (0.038 g, 4%) and 3-allyl-7-methoxycoumarin **5j** (0.057 g, 7%). **6j** was crystallised from diethyl ether–pentane as needles, m.p. 48–49 °C (Found: C, 72.8; H, 5.6. $C_{13}H_{12}O_3$ requires C, 72.21; H, 5.59%); $\delta_H(CDCl_3)$ 3.30 (2 H, d, *J* 7), 3.88 (3 H, s), 5.20 (2 H, m), 5.98 (1 H, m), 6.83 (2 H, m), 7.32 (1 H, d, *J* 8.5) and 7.45 (1 H, s); $\nu_{max}(CHCl_3$, FTIR)/cm^{-1} 1713 and 1616; λ_{max}(EtOH)/nm 208, 214sh and 322 ($\log_{10}\varepsilon$ 4.31, 4.21 and 4.22); *m/z* (EI) 216 (M^+, 100%), 201 (18), 188 (32), 173 (38), 161 (23) and 115 (11). **1j** was crystallised from diethyl ether–pentane as needles, m.p. 134–136 °C (Found: C, 72.4; H, 5.7. $C_{13}H_{12}O_3$ requires C, 72.21; H, 5.59%); $\delta_H(CDCl_3)$ 3.60 (2 H, d, *J* 6), 3.93 (3 H, s), 4.98 (1 H, dd, *J* 1.5, 10), 5.05 (1 H, dd, *J* 1.5, 17), 5.90 (1 H, m), 6.25 (1 H, d, *J* 9.5), 6.85 (1 H, d, *J* 8.5), 7.32 (1 H, d, *J* 8.5) and 7.63 (1 H, d, *J* 9.5); $\nu_{max}(CHCl_3)$/cm^{-1} 1722 and 1609; λ_{max}(EtOH)/nm 208, 214sh, 246, 256 and 320 ($\log_{10}\varepsilon$ 4.31, 4.08, 3.56, 3.59 and 4.13); *m/z* (EI) 216 (M^+, 100%), 201 (20), 187 (21), 173 (23), 159 (11), 145 (17) and 115 (14). **5j** was crystallised from ethyl ethanoate–hexane as needles, m.p. 79–81 °C (Found: C, 72.3; H, 5.7. $C_{13}H_{12}O_3$ requires C, 72.21; H, 5.59%); $\delta_H(CDCl_3)$ 3.38 (2 H, d, *J* 7.5), 3.91 (3 H, s), 5.08 (2 H, m), 5.97 (1 H, m), 6.25 (1 H, d, *J* 9.5), 6.80 (1 H, s), 7.21 (1 H, s) and 7.60 (1 H, d, *J* 9.5); ν_{max}(KBr, FTIR)/cm^{-1} 1728 and 1625; λ_{max}(EtOH)/nm 205, 222, 241sh, 255 and 328 ($\log_{10}\varepsilon$ 4.36, 4.22, 3.72, 4.08 and 4.12); *m/z* (IBEI) 216 (M^+, 100%), 188 (18), 159 (12), 145 (11), 131 (9), 115 (9) and 91 (16).

Methyl 2'-Allyloxy-4'-benzyloxycinnamate **4k**.—Prepared by the method given above for **4d**. Starting materials: methyl 4'-benzyloxy-2'-hydroxycinnamate **3g** (1.01 g, 3.56 mmol), potassium carbonate (2.76 g, 20 mmol), allyl bromide (1.21 g, 10 mmol), acetone (100 cm^3); refluxed for 5 h. The product, methyl 2'-allyloxy-4'-benzyloxycinnamate **4k** (1.11 g, 96%), was crystallised from ethyl ethanoate–hexane as needles, m.p. 67–67.5 °C (Found: C, 74.3; H, 6.2. $C_{20}H_{20}O_4$ requires C, 74.06; H, 6.22%); $\delta_H(CDCl_3)$ 3.79 (3 H, s), 4.57 (2 H, d, *J* 5), 5.08 (2 H, s), 5.30 (1 H, dd, *J* 1.5, 10), 5.42 (1 H, dd, *J* 1.5, 17), 6.07 (1 H, m), 6.44 (1 H, d, *J* 16), 6.52 (1 H, d, *J* 2.5), 6.58 (1 H, dd, *J* 2.5, 8.5), 7.38 (6 H, m) and 7.93 (1 H, d, *J* 16); $\nu_{max}(CHCl_3)$/cm^{-1} 1702, 1626 and 1606; λ_{max}(EtOH)/nm 203, 240, 288sh, 393 and 325 ($\log_{10}\varepsilon$ 4.23, 3.97, 4.03, 4.06 and 4.15); *m/z* (NH_3, DCI) 325 ($M^+ + 1$, 100%), 324 (M^+, 14), 293 (9), 235 (9) and 91 (39).

Thermal Claisen Rearrangement of Methyl 2'-Allyloxy-4'-benzyloxycinnamate **4k**.—Performed by the method given above for **1d**. Starting materials: methyl 2'-allyloxy-4'-benzyloxycinnamate **4k** (0.32 g, 0.99 mmol), diethylaniline (20 cm^3), refluxed for 4 h. Flash chromatography (diethyl ether–pentane, 1:4) afforded 8-allyl-7-benzyloxycoumarin **6k** (0.22 g, 76%), 6-allyl-7-benzyloxycoumarin **1k** (0.017 g, 6%) and 3-allyl-7-benzyloxycoumarin **5k** (0.025 g, 8%). **6k** Was crystallised from diethyl ether–pentane as needles, m.p. 135–136 °C (Found: C, 8.0; H, 5.5. $C_{19}H_{16}O_3$ requires C, 78.07; H, 5.52%); $\delta_H(CDCl_3)$ 3.45 (2 H, d, *J* 7), 5.10 (2 H, m), 5.17 (2 H, s), 6.02 (1 H, m), 6.25 (1 H, d, *J* 9.5), 6.87 (1 H, s), 7.23 (1 H, s), 7.40 (5 H, m) and 7.62 (1 H, d, *J* 9.5); $\nu_{max}(CHCl_3$, FTIR)/cm^{-1} 1718 and 1619; λ_{max}(EtOH)/nm 208, 250, 297sh and 321 ($\log_{10}\varepsilon$ 4.51, 3.60, 3.98 and 4.19); *m/z* (NH_3, DCI) 310 ($M^+ + 18$, 29%), 293 ($M^+ + 1$, 100), 108 (11) and 91 (11). **1k** Was also crystallised from diethyl ether–pentane as needles, m.p. 112.5–113 °C (Found: C, 78.4; H, 5.5. $C_{19}H_{16}O_3$ requires C, 78.07; H, 5.52%); $\delta_H(CDCl_3)$ 3.68 (2 H, d, *J* 7), 5.02 (1 H, dd, *J* 1.5, 10), 5.10 (1 H, dd, *J* 1.5, 17), 5.20 (2 H, s), 6.00 (1 H, m), 6.26 (1 H, d, *J* 9.5), 6.90 (1 H, d, *J* 8.5), 7.30 (1 H, d, *J* 8.5), 7.37 (5 H, m) and 7.63 (1 H, d, *J* 9.5); $\nu_{max}(CHCl_3)$/cm^{-1} 1722 and 1609; λ_{max}(EtOH)/nm 210, 256 and 320 ($\log_{10}\varepsilon$ 4.36, 3.60 and 4.17); *m/z* (NH_3, CI) 293 ($M^+ + 1$, 100%), 203 (20) and 91 (46). **5k** Was also crystallised from diethyl ether–pentane as needles, m.p. 68–71 °C (Found: C, 78.1; H, 5.4. $C_{19}H_{16}O_3$ requires C, 78.07; H, 5.52%); $\delta_H(CDCl_3)$ 3.28 (2 H, dd, *J* 1, 7), 5.13 (2 H, s), 5.22 (2 H, m), 5.98 (1 H, m), 6.92 (2 H, m) and 7.40 (7 H, m); $\nu_{max}(CHCl_3$, FTIR)/cm^{-1} 1730 and 1630; λ_{max}(EtOH)/nm 207, 251, 294sh and 320 ($\log_{10}\varepsilon$ 4.28, 3.40, 3.91 and 4.11); *m/z* (IBEI) 292 (M^+, 16%) and 91 (100).

Methyl 2'-(But-2-enyloxy)-4'-methoxycinnamate **4l**.—Prepared by the method given above for **4d**. Starting materials: methyl 2'-hydroxy-4'-methoxycinnamate **3d** (0.92 g, 4.4 mmol), potassium carbonate (2.76 g, 20 mmol), but-2-enyl bromide (purified by preparative GLC) (0.60 g, 4.4 mmol), acetone (50 cm^3), refluxed for 5 h. Flash chromatography (diethyl ether–pentane, 1:4) afforded methyl 2'-(but-2-enyloxy)-4'-methoxycinnamate **4l** (1.07 g, 93%) which crystallised as needles, m.p. 86–87 °C (Found: 68.85; H, 6.9. $C_{15}H_{18}O_4$ requires C, 68.69; H, 6.92%); $\delta_H(CDCl_3)$ 1.78 (3 H, d, *J* 7), 3.79 (3 H, s), 3.83 (3 H, s), 4.52 (2 H, m), 5.82 (2 H, m), 6.42 (1 H, d, *J* 16), 6.43 (1 H, d, *J* 2.5), 6.47 (1 H, dd, *J* 2.5, 8.5), 7.43 (1 H, d, *J* 8.5) and 7.93 (1 H, d, *J* 16); $\nu_{max}(CHCl_3)$/cm^{-1} 1702, 1626 and 1607; λ_{max}(EtOH)/nm 202, 212sh, 238, 292 and 324 ($\log_{10}\varepsilon$ 3.97, 3.83, 3.81, 3.81 and 3.92) *m/z* (EI) 292 (M^+, 30%), 208 (50), 176 (100), 148 (97), 133 (38) and 121 (11).

Thermal Claisen Rearrangement of Methyl 2'-(But-2-enyloxy)-4'-methoxycinnamate **4l**.—Performed by the method given above for **1d**. Starting materials: methyl 2'-(but-2-enyloxy)-4'-methoxycinnamate **4l** (1.00 g, 3.82 mmol), diethylaniline (20 cm^3), refluxed for 5 h. Flash chromatography (diethyl ether–pentane, 1:4) afforded 7-methoxy-8-(1-methylallyl)coumarin **6l**

(0.47 g, 53%), 6-(but-2-enyl)-7-methoxycoumarin **1l** (0.25 g, 28%) and 3-(but-2-enyl)-7-methoxycoumarin **5l** (0.08 g, 9%). **6l** Was crystallised from diethyl ether–pentane as needles, m.p. 97–98 °C (Found: C, 72.9; H, 6.3. $C_{14}H_{14}O_3$ requires C, 73.03; H, 6.13%); $\delta_H(CDCl_3)$ 1.47 (3 H, d, *J* 7), 3.92 (3 H, s), 4.37 (1 H, m), 4.98 (1 H, dd, *J* 1.5, 10), 5.09 (1 H, dd, *J* 1.5, 17), 6.24 (1 H, d, *J* 9.5), 6.30 (1 H, m), 6.85 (1 H, d, *J* 8.5), 7.30 (1 H, d, *J* 8.5) and 7.62 (1 H, d, *J* 9.5); ν_{max}(KBr disc, FTIR)/cm^{-1} 1733 and 1626; λ_{max}(EtOH)/nm 201, 215, 240 and 216 ($\log_{10}\varepsilon$ 4.11, 4.06, 4.00 and 4.19); *m/z* (IBEI) 230 (M^+, 100%), 215 (78), 199 (10), 187 (18), 159 (20), 131 (15) and 115 (14). **1l** Was also crystallised from diethyl ether–pentane as needles, m.p. 59–61 °C (Found: C, 73.2; H, 6.3. $C_{14}H_{14}O_3$ requires C, 73.03; H, 6.13%); $\delta_H(CDCl_3)$ 1.71 (3 H, d, *J* 5), 3.33 (2 H, d, *J* 6), 3.90 (3 H, s), 5.58 (2 H, m), 6.27 (1 H, d, *J* 9.5), 6.79 (1 H, s), 7.20 (1 H, s) and 7.63 (1 H, d, *J* 9.5); ν_{max}(KBr disc, FTIR)/cm^{-1} 1724 and 1605; λ_{max}(EtOH)/nm 207, 217sh, 246, 256 and 319 ($\log_{10}\varepsilon$ 4.29, 4.02, 3.55, 3.58 and 4.08); *m/z* (IBEI) 230 (M^+, 100%), 215 (81), 199 (24), 187 (38), 159 (41), 131 (18), 128 (12) and 115 (21). **5l** Was also crystallised from diethyl ether–pentane as needles, m.p. 86–88 °C (Found: C, 73.15; H, 6.1. $C_{14}H_{14}O_3$ requires C, 73.03; H, 6.13%); $\delta_H(CDCl_3)$ 1.74 (3 H, d, *J* 5), 3.22 (2 H, d, *J* 6), 3.87 (3 H, s), 5.53 (2 H, m), 6.83 (2 H, m), 7.32 (1 H, d, *J* 8.5) and 7.42 (1 H, s); ν_{max}($CHCl_3$, FTIR)/cm^{-1} 1713 and 1617; λ_{max}(EtOH)/nm 204, 215sh, 252 and 320 ($\log_{10}\varepsilon$ 4.25, 4.04, 3.33 and 4.08); *m/z* (IBEI) 230 (M^+, 100%), 215 (28), 201 (26), 189 (69), 187 (39), 161 (16) and 115 (9).

Methyl 4′-Benzyloxy-2′-(but-2-enyloxy)cinnamate **4m**.—Prepared by the method given above for **4d**. Starting materials: methyl 4′-benzyloxy-2′-hydroxycinnamate **3g** (1.0 g, 3.5 mmol), potassium carbonate (1.38 g, 10 mmol), but-2-enyl bromide (purified by preparative GLC) (0.72 g, 5.3 mmol), acetone (50 cm^3), refluxed for 5 h. Flash chromatography (diethyl ether–pentane, 1:4) afforded methyl 4′-benzyloxy-2′-(but-2-enyloxy)-cinnamate **4m** (1.12 g, 95%) which crystallised from ethyl ethanoate–hexane as needles, m.p. 47–49 °C (Found: C, 74.3; H, 6.5. $C_{21}H_{22}O_4$ requires C, 74.54; H, 6.55%); $\delta_H(CDCl_3)$ 1.75 (3 H, d, *J* 7), 3.79 (3 H, s), 4.50 (2 H, d, *J* 7), 5.10 (2 H, s), 5.78 (1 H, m), 6.42 (1 H, d, *J* 16), 6.52 (1 H, d, *J* 2.5), 6.57 (1 H, dd, *J* 2.5, 8.5), 7.38 (7 H, m) and 7.93 (1 H, d, *J* 16); ν_{max}($CHCl_3$)/cm^{-1} 1701, 1624 and 1606; λ_{max}(EtOH)/nm 203, 240, 288sh, 293 and 326 ($\log_{10}\varepsilon$ 4.24, 3.96, 4.02, 4.04 and 4.13); *m/z* (NH_3, CI) 339 ($M^+ + 1$, 100%) and 91 (26).

Thermal Claisen Rearrangement of Methyl 4′-Benzyloxy-2′-(but-2-enyloxy)cinnamate **4m**.—Performed by the method given above for **1d**. Starting materials: methyl 4′-benzyloxy-2′-(but-2-enyloxy)cinnamate **4m** (0.30 g, 0.98 mmol), diethylaniline (15 cm^3), refluxed for 4 h. Flash chromatography diethyl ether–pentane, 1:4) afforded 7-benzyloxy-8-(1-methylallyl)coumarin **6m** (0.135 g, 50%), 7-benzyloxy-6-(but-2-enyl)coumarin **1m** (0.073 g, 27%) and 7-benzyloxy-3-(but-2-enyl)coumarin **5m** (0.022 g, 8%). **6m** Was crystallised from ethyl ethanoate–hexane as needles, m.p. 110–112 °C (Found: C, 78.5; H, 6.0. $C_{20}H_{18}O_3$ requires C, 78.41; H, 5.92%); $\delta_H(CDCl_3)$ 1.70 (3 H, d, *J* 6), 3.37 (2 H, d, *J* 7), 5.15 (2 H, s), 5.57 (2 H, m), 6.23 (1 H, d, *J* 9.5), 6.84 (1 H, s), 7.22 (1 H, s), 7.53 (5 H, m) and 7.62 (1 H, d, *J* 9.5); ν_{max}($CHCl_3$)/cm^{-1} 1720 and 1620; λ_{max}(EtOH)/nm 203, 218sh, 241, 250, 288sh, 296sh and 325 ($\log_{10}\varepsilon$ 4.54, 4.19, 3.66, 3.54, 3.75, 3.81 and 4.07); *m/z* (NH_3, CI) 307 ($M^+ + 1$, 100%), 217 (10) and 91 (46). **1m** Was crystallised from ethyl ethanoate–hexane as needles, m.p. 103–105 °C (Found: C, 78.45; H, 6.1. $C_{20}H_{18}O_3$ requires C, 78.41; H, 5.92%); $\delta_H(CDCl_3)$ 1.50 (3 H, d, *J* 7), 4.43 (1 H, m), 5.00 (1 H, dd, *J* 2, 9), 5.10 (1 H, dd, *J* 2, 16), 5.18 (2 H, s), 6.23 (1 H, d, *J* 9.5), 6.33 (1 H, m), 6.88 (1 H, d, *J* 8), 7.27 (1 H, d, *J* 8), 7.38 (5 H, m) and 7.60 (1 H, d, *J* 9.5); ν_{max}($CHCl_3$)/cm^{-1} 1720 and 1605; λ_{max}(EtOH)/nm 204, 247sh, 256 and 318 ($\log_{10}\varepsilon$ 4.58, 3.58, 3.58 and 4.11); *m/z* (NH_3, CI) 307 ($M^+ + 1$, 100%), 306 (M^+, 9), 217 (14), 215 (9) and 91 (30). **5m** Was crystallised from ethyl ethanoate–hexane as needles, m.p. 111–114 °C (Found: C, 78.2; H, 6.05. $C_{20}H_{18}O_3$ requires C, 78.41; H, 5.92%); $\delta_H(CDCl_3)$ 1.73 (3 H, d, *J* 6), 3.20 (2 H, d, *J* 6), 5.12 (2 H, s), 5.60 (2 H, m), 6.88 (2 H, m) and 7.38 (7 H, m); ν_{max}(KBr disc, FTIR)/cm^{-1} 1705 and 1618; λ_{max}(EtOH)/nm 204, 250sh, 288sh, 296sh and 321 ($\log_{10}\varepsilon$ 4.47, 3.36, 3.74, 3.84 and 4.05); *m/z* (NH_3, CI) 307 ($M^+ + 1$, 100%), 306 (M^+, 32) and 91 (90).

Methyl 4′-Benzyloxy-2′-hydroxy-5′-(3-methylbut-2-enyl)cinnamate **7**.—Prepared by the method given above for **3d**. Starting materials: 7-benzyloxy-6-(3-methylbut-2-enyl)coumarin **1g** (2.41 g, 7.54 mmol), sodium methoxide solution (2.05 g, in 100 cm^3 of magnesium dried methanol), refluxed for 3 h. The product, methyl 4′-2′-hydroxy-5′-(3-methylbut-2-enyl)cinnamate **7** (2.52 g, 95%), crystallised from ethyl ethanoate–hexane as needles, m.p. 122.5–123.5 °C (Found: C, 75.2; H, 7.0. $C_{22}H_{24}O_4$ requires C, 74.98; H, 6.86%); $\delta_H(CDCl_3)$ 1.63 (3 H, s), 1.75 (3 H, s), 3.28 (2 H, d, *J* 7.5), 3.81 (3 H, s), 5.08 (2 H, s), 5.30 (1 H, m), 5.82 (1 H, s, D_2O exchange), 6.38 (1 H, s), 6.45 (1 H, d, *J* 16), 7.23 (1 H, s), 7.37 (5 H, m) and 7.92 (1 H, d, *J* 16); ν_{max}($CHCl_3$)/cm^{-1} 3310, 1690 and 1610; λ_{max}(EtOH)/nm 204, 222sh, 244, 291sh, 294 and 337 ($\log_{10}\varepsilon$ 4.51, 4.23, 4.10, 4.16, 4.18 and 4.28); *m/z* (NH_3, DCI) 353 ($M^+ + 1$, 64%), 352 (M^+, 35), 321 (23) and 91 (100).

Methyl 4′-Benzyloxy-5′-(3-methylbut-2-enyl) (3-methylbut-2-enyloxy)cinnamate **8**.—Prepared by the method given above for **4d**. Starting materials: methyl 4′-benzyloxy-2′-hydroxy-5′-(3-methylbut-2-enyl)cinnamate **7** (0.99 g, 2.80 mmol), potassium carbonate (2.76 g, 20 mmol), 3-methylbut-2-enyl bromide (2.09 g, 14 mmol), acetone (75 cm^3), refluxed for 4 h. Flash chromatography (diethyl ether–pentane, 1:4) afforded methyl 4′-benzyloxy-5′-(3-methylbut-2-enyl)-2′-(3-methylbut-2-enyloxy)cinnamate **8** 1.12 g, 95%) as a colourless oil (Found: C, 77.1; H, 7.7. $C_{27}H_{32}O_4$ requires C, 77.12; H, 7.67%); $\delta_H(CDCl_3)$ 1.66 (3 H, s), 1.74 (3 H, s), 1.76 (3 H, s), 1.79 (3 H, s), 3.30 (2 H, d, *J* 7), 3.82 (3 H, s), 4.53 (2 H, d, *J* 7), 5.12 (2 H, s), 5.28 (1 H, m), 5.47 (1 H, m), 6.42 (1 H, d, *J* 16), 6.48 (1 H, s), 7.28 (1 H, s), 7.47 (5 H, m) and 7.95 (1 H, d, *J* 16); ν_{max}($CHCl_3$, FTIR)/cm^{-1} 1723, 1629 and 1608; λ_{max}(EtOH)/nm 212, 242, 289sh, 293 and 336 ($\log_{10}\varepsilon$ 4.52, 4.36, 4.34, 4.35 and 4.38); *m/z* (NH_3, DCI) 421 ($M^+ + 1$, 92%), 420 (M^+, 31), 353 (100), 297 (63) and 91 (88).

Thermal Claisen Rearrangement of Methyl 4′-Benzyloxy-5′-(3-methylbut-2-enyl)-2′-(3-methylbut-2-enyloxy)cinnamate **8**.*—Performed by the method given above for **1d**. Starting materials: methyl 4′-benzyloxy-5′-(3-methylbut-2-enyl)-2′-(3-methylbut-2-enyloxy)cinnamate **8** (0.80 g, 1.90 mmol), diethylaniline (15 cm^3), refluxed for 4 h. Flash chromatography (diethyl ether–pentane, 1:4) afforded 7-benzyloxy-3,6-bis(3-methylbut-2-enyl)coumain **9** (0.67 g, 91%) which crystallised from ethyl ethanoate–pentane as needles, m.p. 85–86 °C (Found: C, 80.5; H, 7.35. $C_{26}H_{28}O_3$ requires C, 80.38; H, 7.27%); $\delta_H(CDCl_3)$ 1.67 (3 H, s), 1.70 (3 H, s), 1.77 (3 H, s), 1.82 (3 H, s), 3.22 (2 H, d, *J* 7.5), 3.39 (2 H, d, *J* 7.5), 5.14 (2 H, s), 5.32 (2 H, m), 6.85 (1 H, s), 7.17 (1 H, s), 7.37 (1 H, s) and 7.38 (5 H, m); ν_{max}($CHCl_3$)/cm^{-1} 1705 and 1615; λ_{max}(EtOH)/nm 206,

* The procedure may also be carried out without separation of the 3-and 6-prenylated coumarins resulting from the first rearrangement. Methoxide-induced cleavage and prenylation led to a mixture of **8** and its 3-prenyl isomer, both of which yielded the desired product **9** on thermal rearrangement. The overall yield of balsamiferone from umbelliferone is 55% using this procedure.

222sh, 254sh, 295sh and 327 ($\log_{10}\varepsilon$ 4.60, 4.24, 3.67, 3.91 and 4.18); *m/z* (IBEI) 388 (M^+, 31%), 297 (17) and 91 (100).

Balsamiferone (7-*Hydroxy*-3,6-*bis*(3-*methylbut*-2-*enyl*)*coumarin*) **10**.—Prepared by the method given above for **1a**. Starting materials: 7-benzyloxy-3,6-bis(3-methylbut-2-enyl)-coumarin **9** (0.40 g, 1.03 mmol), boron trichloride (0.60 g, 5.15 mmol, 5.15 cm^3 of a 1 mol dm^{-3} solution in dichloromethane), dichloromethane (20 cm^3), stirred for 1 h at −50 °C. Flash chromatography (diethyl ether–pentane, 1:1) afforded balsamiferone **10** (0.282 g, 92%) which crystallised from ethyl ethanoate–hexane as needles, m.p. 134–136 °C (lit.,[13] 135–137 °C) $\delta_H(CDCl_3)$ 1.75 (3 H, s), 1.77 (3 H, s), 1.78 (6 H, s), 3.20 (2 H, d, *J* 7), 3.36 (2 H, d, *J* 7), 5.29 (2 H, m), 6.20 (1 H, s, D_2O exchange), 6.86 (1 H, s), 7.14 (1 H, s) and 7.37 (1 H, s); $\nu_{max}(CHCl_3$, FTIR)/cm^{-1} 3684, 1703 and 1619; λ_{max}(EtOH)/nm 206, 219sh, 246sh, 257, 304sh and 332 ($\log_{10}\varepsilon$ 4.44, 4.11, 3.89, 3.52, 3.82 and 4.12); *m/z* (IBEI) 298 (M^+, 47%), 283 (18), 243 (100), 149 (9) and 91 (12).

6-(3-*Methylbut*-2-*enyl*)-7-(3-*methylbut*-2-*enyloxy*)*coumarin* **11**.—Prepared by the method given above for **4d**. Starting materials: demethylsuberosin **1a**) (0.50 g, 2.17 mmol), potassium carbonate (1.38 g, 10 mmol), 3-methylbut-2-enyl bromide (0.75 g, 5.0 mmol), acetone (50 cm^3), refluxed for 4 h. Flash chromatography (diethyl ether–pentane, 1:4) afforded 6-(3-methylbut-2-enyl)-7-(3-methylbut-2-enyloxy)coumarin **11** (0.063 g, 97%) which crystallised as needles, m.p. 78–79 °C (Found: C, 76.6; H, 7.4. $C_{19}H_{22}O_3$ requires C, 76.45; H, 7.43%); $\delta_H(CDCl_3)$ 1.71 (3 H, s), 1.77 (6 H, s), 1.82 (3 H, s), 3.32 (2 H, d, *J* 7.5), 4.61 (2 H, d, *J* 7.5), 5.29 (1 H, m), 5.48 (1 H, m), 6.24 (1 H, d, *J* 9.5), 6.77 (1 H, s), 7.17 (1 H, s) and 7.61 (1 H, d, *J* 9.5); $\nu_{max}(CHCl_3$, FTIR)/cm^{-1} 1718 and 1619; λ_{max}(EtOH)/nm 205, 222, 254, 296sh and 331 ($\log_{10}\varepsilon$ 4.54, 4.29, 3.69, 3.89 and 4.19) *m/z* (IBEI) 298 (M^+, 7%), 230 (82) and 175 (100).

Thermal Claisen Rearrangement of 6-(3-*Methylbut*-2-*enyl*)-7-(3-*methylbut*-2-*enyloxy*)*coumarin* **11**.—Performed by the method given above for **1d**. Starting materials: 6-(3-methylbut-2-enyl)-7-(3-methylbut-2-enyloxy)coumarin **11** (0.253 g, 0.85 mmol), diethylaniline (15 cm^3), refluxed for 3 h. Flash chromatography (diethyl ether–pentane, 1:4) afforded gravelliferone [3-(1,1-dimethylallyl)-7-hydroxy-6(3-methylbut-2-enyl)coumarin] **12** (0.051 g, 20%), 2′,2′,3′-trimethyl-6-(3-methylbut-2-enyl)-angelicin[3-(1,1-dimethylallyl)-8,9,9-trimethyl-6-(3-methylbut-2-enyl)-8,9-dihydro-2*H*-furo[2,3-*h*]-1-benzopyran-2-one **13** (0.017 g, 7%) and recovered demethylsuberosin **1a**) (0.11 g, 56%). **12** Was crystallised from ethyl ethanoate–hexane as needles, m.p. 165–167 °C (lit.,[14] 166–168 °C); $\delta(CDCl_3)$ 1.49 (6 H, s), 1.76 (3 H, s), 1.81 (3 H, s), 3.38 (2 H, d, *J* 7.5), 5.08 (1 H, d, *J* 17), 5.10 (1 H, d, *J* 10), 5.32 (1 H, m), 6.18 (1 H, dd, *J* 10, 17), 6.66 (1 H, br s), 6.95 (1 H, s), 7.17 (1 H, s), and 7.52 (1 H, s); $\nu_{max}(CHCl_3)$/cm^{-1} 3698 and 1708; λ_{max}(EtOH)/nm 210, 219sh, 245, 250, 296sh, 309sh and 333 ($\log_{10}\varepsilon$ 4.21, 4.07, 3.53, 3.69, 3.70, 3.78 and 4.00); *m/z* (IBEI) 298 (M^+, 76%), 283 (100), 243 (92), 215 (16), 199 (14) and 128 (10). **13** Was crystallised from ethyl ethanoate–hexane as needles, m.p. 135–139 °C (Found: C, 76.5; H, 7.8. $C_{19}H_{22}O_3$ requires C, 76.45; H, 7.43%); $\delta_H(CDCl_3)$ 1.39 (3 H, d, *J* 6), 1.45 (6 H, s), 1.74 (3 H, s), 1.80 (3 H, s), 3.27 (2 H, d, *J* 7), 3.33 (1 H, q, *J* 6), 5.30 (1 H, m), 6.17 (1 H, d, *J* 9.5), 7.03 (1 H, s) and 7.59 (1 H, d, *J* 9.5); $\nu_{max}(CHCl_3)$/cm^{-1} 3435, 1718 and 1610; λ_{max}(EtOH)/nm 211, 217sh, 252, 260 and 332 ($\log_{10}\varepsilon$ 4.19, 4.05, 3.62, 3.59 and 3.91) *m/z* (IBEI) 298 (M^+, 77%), 258 (35), 230 (100) and 103 (32).

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