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Syntheses of 6-Acylcoumarins *via* highly Regioselective Fries Rearrangements. Total Syntheses of the Linear Acylated Coumarins Geijerin And Dehydrogeijerin.†

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Abstract: Methyl 3-(2-acyloxy-4-methoxyphenyl)propanoates (**7**), prepared in high yield from 7-methoxycoumarin are key intermediates in general and efficient syntheses of 6-acylcoumarins. Under standard Fries rearrangement conditions (**7**) undergo highly regioselective *para*-migration with aluminium chloride in nitromethane. The resulting *C*-acylated products (**8**) are converted into 6-acyl-7-methoxycoumarins (**4**). The scope and limitations of the rearrangement and the application to the total syntheses of the natural linear acylcoumarins, geijerin (**4a**) and dehydrogeijerin (**4b**), are described.

Of all the isolated natural coumarins[1] only a minority have an acyl group attached to the aromatic coumarin skeleton. The mammeins which are fully substituted in the carbocycle and have an acyl group at either C-6 or C-8, constitute the majority of such compounds. In the syntheses of mammeins, Crombie *et al.* usually introduce the acyl fragment by forming phenyl ketones under Friedel Crafts conditions before constructing the coumarin nucleus.[2] Only a handful of coumarins of the non-mammea type have been isolated that possess an acyl fragment attached to the carbon skeleton and in such cases the acyl group is almost exclusively derived from an isoprenoid modification. Two of the three known non-mammea natural coumarins possessing a 3-methyl-2-butenoyl (senecioyl) side chain have been elegantly synthesised by Murray and co-workers. In the first synthesis, gabralactone (**2**), was prepared by a base-induced double ring opening of the angular pyranocoumarin (**1**), producing the senecioyl group at the desired angular position as a consequence of relactonisation occurring onto the alternative *ortho*-hydroxy group on subsequent reacidification.[3] The second example, 7-methoxy-8-senecioylcoumarin (**3**),[4] was synthesised by a completely different approach in which the senecioyl group was introduced by coupling a protected hydroxy copper acetylide to 8-iodo-7-methoxycoumarin[5] followed by isomerisation of the deprotected carbinol to the desired conjugated enone.[6] The first total syntheses of the non-mammea natural coumarins, geijerin (**4a**) and dehydrogeijerin (**4b**), is described in this text.[7]

† Dedicated to Professor Charles W. Rees on the occasion of his retirement from the Hoffman Chair, Imperial College London.

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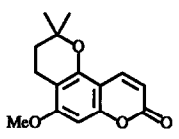

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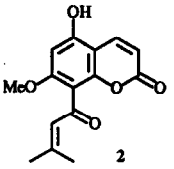

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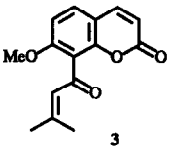

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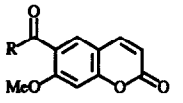

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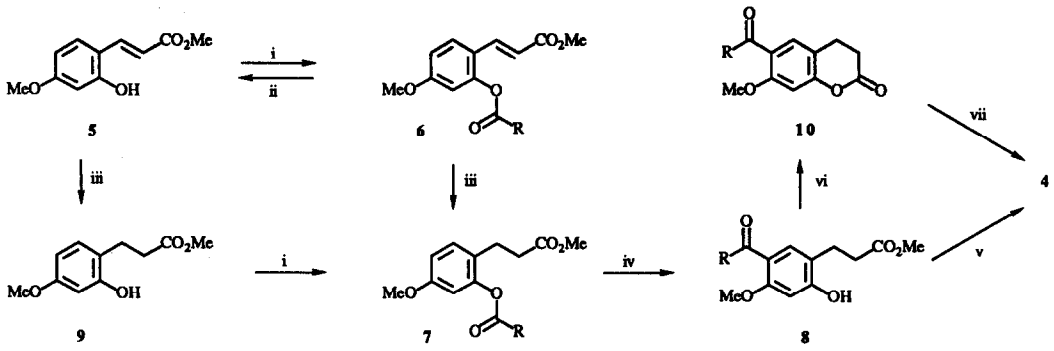
a R= $(CH_3)_2CHCH_2$-

b R=$(CH_3)_2C$=CH-

As the overwhelming majority of natural coumarins are derivatives of umbelliferone (7–hydroxycoumarin), introduction of an acyl group at C-6 or C-8 of this nucleus would appear at first sight to present the most direct means of constructing these systems. However, Friedel Crafts acylation and its intra-molecular counterpart, the Fries rearrangement, have both been shown to be synthetically ineffective for umbelliferone derivatives. This is most probably due to the electron withdrawing effect of the benzannelated pyrone system. In support of this view, Friedel Crafts acylation has been shown to occur in modest yield when the electron withdrawing effect is removed by reducing the pyrone double bond to afford a 3,4-dihydrocoumarin.[8] Fries rearrangement of 7-acetoxycoumarin has been reported to occur, but gives only a very low yield of 8-acetylumbelliferone together with traces of 6-acetylumbelliferone.[9]

We have previously demonstrated successful Lewis acid catalysed *ortho*-Claisen rearrangements with substrates in which the coumarin ring has been cleaved,[10] when the migrating allyl group can be considered to possess some cationic nature,[11] and thus show some mechanistic analogy with the Fries rearrangement. Therefore, we decided to investigate Fries rearrangements of related substrates (**6**) and (**7**) in order to ascertain if such rearrangements could be achieved and if they would occur in a regioselective manner.

7–methoxycoumarin was cleaved to the 2'-hydroxy-4'-methoxycinnamate ester (**5**) and the phenol group acetylated (Ac_2O, pyridine). Unfortunately, all attempts at rearrangement of the product (**6c**) led to deacetylation of the starting material, presumably due to the electron withdrawing nature of the conjugated ester. In order to increase the electron density of the aromatic ring, (**6c**) was reduced to methyl 3–(2–acetoxy–4–methoxyphenyl)propanoate (**7c**) by hydrogenation at atmospheric pressure over 5% palladium on charcoal. In this instance, subsequent rearrangement of (**7c**) using 5 equivalents of aluminium chloride predissolved in nitromethane[12] occurred smoothly, enabling the desired product, methyl 3–(5–acetyl–2–hydroxy–4–methoxyphenyl) propanoate (**8c**) to be isolated in 71% yield with no isomeric products being detected in the crude reaction mixture (**Scheme**). The substitution pattern of the aromatic ring was clearly indicated by the appearance of two 1H singlets in the ^{1}HNMR spectrum of (**8c**) at δ 6.51 and 7.45, indicating their *para*–relationship. The mildness of the reaction conditions compared to those commonly used to effect Fries rearrangements is particularly noteworthy and is presumably the reason for absence of any *ortho*–rearranged product, the formation of which is favoured by high reaction temperatures.[13] Other combinations of Lewis acids and solvents led either to complete deacylation or to recovery of starting material, with the exception of aluminium chloride in nitrobenzene which also gave the desired rearrangement but proved much less convenient to use. In both successful instances it was observed that addition of the aluminium chloride to the solvent led to the appearance of an orange solution and it therefore seems that the solvent plays an important rôle in generating the active catalyst.



(a) R = $(CH_3)_2CHCH_2$
(b) R = $(CH_3)_2C{=}CH$
(c) R = CH_3
(d) R = CH_3CH_2
(e) R = $(CH_3)_2CH$
(f) R = Ph
(g) R = $(CH_3)_3C$
(h) R = H

Reagents and conditions: (i) RCOCl or $(RCO)_2O$, pyridine, 20°C; (ii) Lewis acid, (iii) H_2, 5%Pd-C; (iv) $AlCl_3$ (5 equiv.), $MeNO_2$, 20°C; (v) Ph_2O, 5%Pd-C, reflux; (vi) Ph_2O, reflux; (vii) Ph_2O, 1-dodecene (5 equiv.), 5%Pd-C, reflux.

Scheme

Similar results were obtained for a range of precursors (**7a–f, Table**) prepared by the same procedure, with the exception of the senecioyl ester (**7b**), the preparation of which necessitated initial reduction of (**5**) to (**9**)before acylation of the phenol to furnish (**7b**). Increasing α-substitution of the acyl groups, as in (**7e, g**) resulted in reduced yields of rearrangement products, with the benzoate ester giving 17% yield of rearranged material and the pivalate ester (**7g**) undergoing total deacylation. The increasing competition from deacylation is probably due to a combination of increased steric bulk of the acyl groups and the increasing ease of decomposition of the acylium species. The latter rationale applies equally to methyl 3-(2-formyl-4-methoxyphenyl)propanoate (**7h**) which underwent total deformylation on attempted rearrangement.

	Isolated Yield %				
	(6)	(7)	(8)	(10)	(4)
a	§	96	65	58	66
b	84	95	73	84	10
c	100	100	71	¶	70
d	99	100	62	83	50
e	77	95	35	¶	54
f	§	85	17	¶	64
g	90	100	0	–	–
h	§	93	0	–	–

§ compound not prepared ¶ Intermediate not isolated

Table

Attempts to introduce acyl groups by direct Friedel-Crafts acylation of (**9**) with the requisite acyl chloride using aluminium chloride in nitromethane also led to the desired products (**8**) but in inferior yields to those obtained under Fries rearrangement conditions.

Concomitant lactone formation and dehydrogenation of the rearranged products to form the 6-acyl-7-methoxycoumarins (**4**) was conveniently carried out in most cases by refluxing in diphenyl ether in the presence of 5%Pd-C. However, in the case of (**8b**), the senecioyl side chain acted as an intramolecular hydrogen acceptor furnishing geijerin (**4a**), previously isolated from *Geijera salcifolia*.[14] This was more efficiently synthesised from 7-methoxycoumarin in 40% yield over 5 steps *via* rearrangement of the 3-methylbutanoyl aryl ester (**7a**), followed by the usual oxidative ring closure with 5% Pd-C in diphenyl ether at reflux. Dehydrogeijerin (**4b**), identified in extracts of *Geijera. parviflora*[15] and *Amyris madrensis*,[16] was obtained from (**8b**), albeit in only 10% yield , by first isolating the dihydrocoumarin intermediate (**10b**) and then treating this with 5% Pd-C in the presence of 1-dodecene to act as a competing hydrogen acceptor.[17]

In summary, 6-acylated umbelliferone derivatives have been prepared in good overall yield and with very high regioselectivity from 3-(2-acyloxy-4-methoxyphenyl)propanoic acid derivatives by a key aluminium chloride–nitromethane mediated *para*–Fries rearrangement. This strategy has been applied to the total syntheses of the naturally occurring linear acylated coumarins geijerin (**4a**) and dehydrogeijerin (**4b**) in 40% and 6% overall yields respectively from 7-methoxycoumarin.

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EXPERIMENTAL

General Methods. Melting points were determined with a Kofler hot stage apparatus and are uncorrected. 300MHz ^{1}HNMR spectra of solutions in $CDCl_3$ were recorded on a Bruker WH300 spectrometer. Chemical shifts (δ) are reported as parts per million downfield from tetramethylsilane and data are reported as: chemical shift, integration, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; qn, quintet; m, multiplet) and coupling constant. IR spectra were recorded on Perkin-Elmer 297 and 781 spectrometers or a 1750 FTIR spectrometer. UV spectra were recorded on a Perkin-Elmer 555 spectrophotometer and data are reported as: λ_{max} (ε). Mass spectra were recorded on V.G. Micromass 16F and 30F spectrometers using electron impact ionisation (EI), in beam electron impact ionisation (IBEI), chemical ionisation with ammonia (CI) or desorption chemical ionisation (DCI) and data are quoted as: peak position (relative intensity %). Flash column chromatography was performed by the method of Still[18] and dry flash chromatography by the method of Harwood.[19] TLC analyses were performed using Merck Kieselgel 60 F_{254} plates, which were first observed under UV light (254 and 366nm) and then stained with iodine vapour. All starting materials and reagents were purchased from the Aldrich Chemical Company.

Methyl 2'-hydroxy-4'-methoxycinnamate (5). 7-Methoxycoumarin (8.00g, 46mmol), was added to a freshly prepared solution of sodium methoxide (5.40g, 100mmol) in magnesium dried methanol (300ml) and refluxed for 5h under nitrogen.(***NOTE*** It is important to prepare the sodium methoxide immediately before use. Aged reagent was consistently observed to give no ring–opened material, probably due to traces of sodium hydroxide strongly accelerating recyclisation to starting material). The cooled solution was then carefully neutralised with 2M HCl, the resulting precipitate extracted into ethyl acetate (100ml), the solution washed with brine until neutral and dried over anhydrous magnesium sulphate. Removal of the solvent *in vacuo* afforded methyl 2'-hydroxy-4'-methoxycinnamate (**5**), which was obtained as needles from ethyl acetate / hexane (8.73g, 92%), mp 144-146.5°C. (Found: C, 63.30%; H, 5.90%. $C_{11}H_{12}O_4$ requires: C, 63.46%; H, 5.81%). ^{1}HNMR ($CDCl_3$): δ 3.80 (3H, s), 3.82 (3H, s), 6.42 (1H, d, J=2.5Hz), 6.48 (1H, dd, J=2.5, 8.5Hz), 6.53 (1H, d, J=16Hz), 7.08 (1H, bs), 7.38 (1H, d, J=8.5Hz) and 7.98 (1H, d, J=16Hz). υ_{max} ($CHCl_3$): 3590, 1697 and 1612 cm^{-1}. λ_{max} (CCl_4): 292 (13490) 320 (14790) nm. $^m/_z$ (IBEI): 208 (M^+, 70), 176 (71), 148 (100), 133 (51) and 121 (16).

Methyl 3-(2-hydroxy-4-methoxyphenyl)propanoate (9). Methyl 2'-hydroxy-4'-methoxycinnamate (**5**) (4.33g, 20.8mmol), was dissolved in ethyl acetate (200ml) and 5% Pd-C (0.4g) was added cautiously to the solution. The mixture was stirred under hydrogen at ambient temperature and pressure for 1h when

hydrogen uptake ceased. Filtration through a pad of Celite® and evaporation of the solvent afforded methyl 3-(2-hydroxy-4-methoxyphenyl)propanoate (**9**) (4.35g, quant.) which was obtained as needles from ethyl acetate / hexane, mp 90-92°C (lit. 88-89°C).[20] ^{1}HNMR ($CDCl_3$): δ 2.70 (2H, t, J=7Hz), 2.85 (2H, t, J=7Hz), 3.70 (3H, s), 3.77 (3H, s), 6.47 (2H, m), 6.98 (1H, d, J=8.5Hz) and 7.34 (1H, s). υ_{max} ($CHCl_3$): 3322, 1710, 1620 and 1583 cm^{-1}. λ_{max} (EtOH): 205 (19500), 221 (7590), 278 (2820) and 280 (2630) nm. $^m/_z$ (NH_3, CI): 211 (MH^+, 34), 196 (100) and 178 (38).

Methyl 4'-methoxy-2'-senecioyloxycinnamate (6b). Methyl 2'-hydroxy-4'-methoxycinnamate (**5**) (4.25g, 20.4mmol) was dissolved in pyridine (10ml) and this solution added to a solution of senecioyl chloride (3.63g, 30.7mmol) in pyridine (10ml). The mixture was stirred at 20°C under nitrogen for 10h and evaporation to dryness in *vacuo* followed by flash chromatography (1:4 diethyl ether / pentane) afforded methyl 4'-methoxy-2'-senecioyloxycinnamate (**6b**) (4.95g, 84%), obtained as needles from ethyl acetate / hexane, mp 60-61°C. (Found: C, 66.10%; H, 6.20%. $C_{16}H_{18}O_5$ requires: C, 66.20%; H, 6.25%). ^{1}HNMR ($CDCl_3$): δ 2.03 (3H, d, J=1Hz), 2.24 (3H, d, J=1Hz), 3.78 (3H, s), 3.82 (3H, s), 6.00 (1H, m), 6.33 (1H, d, J=16Hz), 6.66 (1H, d, J=2.5Hz), 6.82 (1H, dd, J=2.5, 8.5Hz), 7.58 (1H, d, J=8.5Hz) and 7.92 (1H, d, J=16Hz). υ_{max} ($CHCl_3$): 1720 1640 and 1610 cm^{-1}. λ_{max} (EtOH): 212 (16600), 230 (19050) and 307 (16220) nm. $^m/_z$ (IBEI): 290 (M^+, 9), 212 (18), 208 (13), 180 (16), 166 (22), 151 (46), 148 (21), 125 (28) and 83 (100).

Methyl 2'-acetoxy-4'-methoxycinnamate (6c). Methyl 2'-hydroxy-4'-methoxycinnamate (**5**) (2.00g, 9.6mmol) was dissolved in a mixture of acetic anhydride (5ml) and pyridine (10ml) and stirred at 20°C for 2h under nitrogen. Evaporation to dryness afforded methyl 2'-acetoxy-4'-methoxycinnamate (**6c**) (2.40g, quant.) recrystallised as needles from diethyl ether / pentane, mp 85.5-87°C. (Found: C, 62.5%; H, 5.6%. $C_{13}H_{14}O_5$ requires: C, 62.39%; H, 5.64%). ^{1}HNMR ($CDCl_3$): δ 2.36 (3H, s), 3.78 (3H, s), 3.82 (3H, s), 6.32 (1H, d, J=16Hz), 6.65 (1H, d, J=2.5Hz), 6.80 (1H, dd, J=2.5, 8.5Hz), 7.55 (1H, d, J=8.5Hz) and 7.68 (1H, d, J=16Hz). υ_{max} ($CHCl_3$): 1763, 1708, 1630 and 1611 cm^{-1}. λ_{max} (EtOH): 209 (10000), 229 (10720), 294 (14790) and 307 (14790) nm. $^m/_z$ (NH_3, CI): 268 (MNH_4^+, 100), 251 (MH^+, 76%), 208 (41), 177 (31) and 148 (18).

Methyl 4'-methoxy-2'-propanoyloxycinnamate (6d). Methyl 2'-hydroxy-4'-methoxycinnamate (**5**) (3.70g, 17.8mmol) was stirred in a solution of propionic anhydride (5ml) and pyridine (10ml) at 20°C under nitrogen for 5h. Evaporation to dryness *in vacuo* followed by flash chromatography (1:4 diethyl ether / pentane) afforded methyl 4'-methoxy-2'-propanoyloxycinnamate (**6d**) (4.66g, 99%) as a colourless oil. (Found: C, 63.57%; H, 6.16%. $C_{14}H_{16}O_5$ requires: C, 63.63%; H, 6.10%). ^{1}HNMR ($CDCl_3$): δ 1.32 (3H, t, J=7Hz), 2.66 (2H, q, J=7Hz), 3.79 (3H, s), 3.82 (3H, s), 6.30 (1H, d, J=16Hz), 6.47 (1H, dd, J=2.5, 8.5Hz), 6.65 (1H, d, J=2.5Hz), 7.57 (1H, d, J=8.5Hz) and 7.68 (1H, d, J=16Hz). υ_{max} ($CHCl_3$): 1760, 1708, 1630 and 1612 cm^{-1}. λ_{max} (EtOH): 202 (11220), 228 (9770), 295 (15850) and 305 (15850) nm. $^m/_z$ (EI): 264 (M^+, 20), 208 (76), 176 (100), 148 (99) and 133 (44).

Methyl 2'-isobutanoyloxy-4'-methoxycinnamate (6e). Methyl 2'-hydroxy-4'-methoxycinnamate (**5**) (3.91g, 18.8mmol) was dissolved in a mixture of isobutyric anhydride (3.16g, 20mmol) and pyridine (10ml) and stirred under nitrogen for 5h. Diethyl ether (100ml) was added and the mixture washed with 5M hydrochloric acid (3x25ml) and then with brine until neutral. The organic extract was dried over anhydrous magnesium sulphate, filtered, and the solvent revomed *in vacuo*. The residue was subjected to flash chromatography (1:2 diethyl ether / pentane) affording methyl 2'-isobutanoyloxy-4'-methoxycinnamate (**6e**) (4.00g, 77%) as a colourless oil. (Found: C, 64.75%; H, 6.61%. $C_{15}H_{18}O_5$ requires: C, 64.74%; H, 6.52%). ^{1}HNMR ($CDCl_3$): δ 1.37 (6H, d, J=7Hz), 2.89 (1H, qn, J=7Hz), 3.77 (3H, s), 3.81 (3H, s), 6.32 (1H, d, J=16Hz), 6.62 (1H, d, J=2.5Hz), 6.82 (1H, dd, J=2.5, 9Hz), 7.55 (1H, d, J=9Hz) and 7.70 (1H, d, J=16Hz). υ_{max} ($CHCl_3$): 1756, 1709, 1630, 1601 and 1575 cm^{-1}. λ_{max} (EtOH): 198 (2570), 224 (2240), 291 (3470) and 302 (3470) nm. $^m/_z$ (NH_3, CI): 296 (MNH_4^+, 100), 279 (MH^+, 80), 208 (25) and 177 (28).

Methyl 4'-methoxy-2'-pivaloyloxycinnamate (6g). Methyl 2'-hydroxy-4'-methoxycinnamate (**5**) (0.36g, 1.75mmol) was dissolved in pyridine (5ml) and added in one portion to a stirred solution of pivaloyl chloride (0.21g, 1.8mmol) in pyridine (10ml). The mixture was stirred under nitrogen at 20°C for 8h. Evaporation to dryness *in vacuo* followed by flash chromatography (1:4 diethyl ether / pentane) afforded methyl 4'-methoxy-2'-pivaloyloxycinnamate (**6g**) (0.46g, 90%) as a colourless oil. (Found: C, 65.46%; H, 7.18%. $C_{16}H_{22}O_5$ requires: C, 65.74%; H, 6.90%). ^{1}HNMR ($CDCl_3$): δ 1.43 (9H, s), 3.78 (3H, s), 3.83 (3H, s), 6.32 (1H, d, J=16Hz), 6.58 (1H, d, J=2.5Hz) 6.82 (1H, dd, J=2.5, 16Hz), 7.57 (1H, d, J=9Hz) and 7.80 (1H, d, J=16Hz). υ_{max} ($CHCl_3$): 1750, 1708 1630 and 1612 cm^{-1}. λ_{max} (EtOH): 203 (9770), 224 (8320), 294 (1230) and 307 (1230) nm. $^m/_z$ (NH_3 CI): 310 (MNH_4^+, 48), 293 (MH^+, 100), 261 (12), 208 (25) 176 (29) and 148 (15).

Methyl 3-(2-isovaleryl-4-methoxyphenyl)propanoate (7a). Methyl 3-(2-hydroxy-4-methoxyphenyl)propanoate (**9**) (1.61g, 7.6mmol) was dissolved in benzene (50ml), added to a solution of isovaleryl chloride (0.95g, 7.9mmol) in benzene (50ml) and the mixture refluxed under nitrogen for 5h. After cooling, the solvent was removed *in vacuo* and the residual yellow oil subjected to flash chromatography (1:3 diethyl ether / pentane) affording methyl 3-(2-isovaleryl-4-methoxyphenyl)propanoate (**7a**) (2.17g, 96%) as a colourless oil. (Found: C, 65.59%; H, 7.69%. $C_{16}H_{22}O_5$ requires: C, 65.29%; H, 7.53%). ^{1}HNMR ($CDCl_3$): δ 1.07 (6H, d, J=7Hz), 2.27 (1H, m), 2.48 (2H, d, J=7Hz), 2.55 (2H, m), 2.80 (2H, m), 3.67 (3H, s), 3.78 (3H, s), 6.58 (1H, d, J=2.5Hz), 6.75 (1H, dd, J=2.5, 8.5Hz) and 7.15 (1H, d, J=8.5Hz). υ_{max} ($CHCl_3$): 1740, 1619 and 1583 cm^{-1}. λ_{max} (EtOH): 201 (14130), 222 (8510), 273 (180) and 280 (1580) nm. $^m/_z$ (NH_3, DCI): 312 (MNH_4^+, 100), 295 (MH^+, 55), 210 (43), 196 (23), 178 (26), 137 (13) and 102 (16).

Methyl 3-(4-methoxy-2-senecioyloxyphenyl)propanoate (7b). Methyl 3-(2-hydroxy-4-methoxyphenyl)propanoate (**9**) (2.2g, 10.4mmol) was dissolved in benzene (50ml), added to a solution of senecioyl chloride (1.49g, 12.6mmol) in benzene (50ml) and the mixture was refluxed for 7h under nitrogen. After cooling, the solvent was removed *in vacuo* and the residual oil subjected to flash chromatography (1:8 diethyl ether / pentane) affording methyl 3-(4-methoxy-2-senecioyloxyphenyl)propanoate (**7b**) (2.90g, 95%) as a colourless oil. (Found: C, 65.71%; H, 7.04%. $C_{16}H_{20}O_5$ requires: C, 65.74%; H, 6.90%). ^{1}HNMR ($CDCl_3$): δ 2.00 (3H, d, J=1Hz), 2.24 (3H, d, J=1Hz), 2.58 (2H, t, J=8Hz), 2.82 (2H, t, J=8Hz), 3.66 (3H, s), 3.77 (3H, s), 5.94 (1H, m), 6.62 (1H, d, J=2.5Hz), 6.75 (1H, dd, J=2.5, 8.5Hz) and 7.15 (1H, d, J=8.5Hz). υ_{max} ($CHCl_3$): 1725 and 1640 cm^{-1}. λ_{max} (EtOH): 201 (16600), 221 (20890), 273 (2000) and 280 (2400) nm. $^m/_z$ (IBEI): 392 (M^+, 14), 210 (11), 83 (100).

Methyl 3-(2-acetoxy-4-methoxyphenyl)propanoate (7c). Methyl 2'-acetoxy-4'-methoxycinnamate (**6c**) (0.36g, 1.44mmol) was dissolved in ethyl acetate (100ml) and 5% Pd-C (0.04g) was added cautiously to the solution. The mixture was stirred under hydrogen at ambient temperature and pressure for 0.5h when hydrogen uptake ceased. Filtration and evaporation of the solvent afforded methyl 3-(2-acetoxy-4-methoxyphenyl)propanoate (**7c**) (0.36g, quant.) as a colourless oil. (Found: C, 61.90%; H, 6.48%. $C_{13}H_{16}O_5$ requires: C, 61.93%; H, 6.40%). ^{1}HNMR ($CDCl_3$): δ 2.33 (3H, s), 2.55 (2H, m), 2.80 (2H, m), 3.66 (3H, s), 3.76 (3H, s), 6.60 (1H, d, J=2.5Hz), 6.75 (1H, dd, J=2.5, 8.5Hz) and 7.15 (1H, d, J=8.5Hz). υ_{max} ($CHCl_3$): 1740, 1620 and 1582 cm^{-1}. λ_{max} (EtOH): 202 (13800), 222 (9120), 273 (1900) and 280 (1350) nm. $^m/_z$ (EI): 252 (M^+, 14), 210 (57), 178 (94), 150 (18) and 137 (100).

Methyl 3-(4-methoxy-2-propanoyloxyphenyl)propanoate (7d). Methyl 3-(2-hydroxy-4-methoxy phenyl)propanoate (**9**) (0.10g, 0.48mmol) was dissolved in propionic anhydride (2ml) and pyridine (10ml) and the mixture stirred for 3h under nitrogen. Evaporation to dryness *in vacuo* followed by flash chromatography (1:9 diethyl ether / pentane) afforded methyl 3-(4-methoxy-2-propanoyloxyphenyl) propanoate (**7d**) (0.128g, quant.) as a colourless oil. (Found: C, 62.82%; H, 6.92%. $C_{14}H_{18}O_5$ requires: C, 63.15%; H, 6.81%). ^{1}HNMR ($CDCl_3$): δ 1.29 (3H, t, J=7Hz), 2.53 (2H, t, J=8Hz), 2.63 (2H, q, J=7Hz), 2.78 (2H, t, J=8Hz), 3.65 (3H, s), 3.76 (3H, s), 6.60 (1H, d, J=2.5Hz), 6.73 (1H, dd, J=2.5, 8.5Hz) and 7.13 (1H, d, J=8.5Hz). υ_{max} ($CHCl_3$): 1741, 1620 and 1583 cm^{-1}. λ_{max} (EtOH): 202 (15490), 222 (10000), 274 (2140) and 280 (1950) nm. $^m/_z$ (IBEI): 266 (M^+, 29), 210 (72), 178 (100), 150 (41) and 137 (82).

Methyl 3-(2-isobutanoyloxy-4-methoxyphenyl)propanoate (7e). Methyl 3-(2-hydroxy-4-methoxy phenyl)propanoate (**9**) (1.35g, 6.42mmol) was added to a stirred solution of pyridine (20ml) containing isobutyric anhydride (1.01g, 6.42mmol) and the solution was stirred under nitrogen for 24h. Removal of the solvent *in vacuo* followed by flash chromatography (1:3 diethyl ether / pentane) afforded methyl 3-(2-isobutanoyloxy-4-methoxyphenyl)propanoate (**7e**) (1.71g, 95%) as a colourless oil. (Found: C, 64.53%; H, 7.44%. $C_{15}H_{20}O_5$ requires: C, 64.27%; H, 7.19%). ^{1}HNMR ($CDCl_3$): δ 1.36 (6H, d, J=6.9Hz), 2.55 (2H, t, J=8Hz), 2.80 (2H, t, J=8Hz), 2.82 (1H, q, J=6.9Hz), 3.66 (3H, s), 3.77 (3H, s), 6.58 (1H, d, J=2.6Hz), 6.75 (1H, dd, J=2.6, 8.5Hz) and 7.15 (1H, d, J=8.5Hz). υ_{max} ($CHCl_3$): 1750, 1735, 1620 and 1583 cm^{-1}. λ_{max} (EtOH): 204 (9120), 222 (7940), 274 (1740) and 280 (1550) nm. $^m/_z$ (NH_3, DCI): 298 (MNH_4^+, 100), 281(MH^+, 66), 210 (37), 196 (17), 178 (24) and 137 (14).

Methyl 3-(2-benzoyloxy-4-methoxyphenyl)propanoate (7f). Methyl 3-(2-hydroxy-4-methoxy phenyl)propanoate (**9**) (1.50g, 7.14mmol) was dissolved in benzene (50ml). This solution was added to a solution of benzoyl chloride (5ml) in benzene (50ml) and the mixture was refluxed for 6h under nitrogen. After cooling, the solvent was removed *in vacuo* and the residual oil subjected to flash chromatography (1:8 diethyl ether / pentane) affording methyl 3-(2-benzoyloxy-4-methoxyphenyl)propanoate (**7f**) (1.90, 85%) as a colourless oil. (Found: C, 68.67%; H, 5.79%. $C_{18}H_{18}O_5$ requires: C, 68.78%; H, 5.77%). ^{1}HNMR ($CDCl_3$): δ 2.62 (2H, t, J=7.7Hz), 2.88 (2H, t, J=7.7Hz), 3.62 (3H, s), 3.80 (3H, s), 6.75 (1H, d, J=2.5Hz), 6.80 (1H, dd, J=2.5, 8.5Hz), 7.22 (1H, d, J=8.5Hz), 7.53 (2H, t, J=8Hz), 7.65 (1H, t, J=8Hz)

and 8.23 (2H, d, J=8Hz). υ_{max} ($CHCl_3$): 1734, 1620 and 1583 cm^{-1}. λ_{max} (EtOH): 202 (20420), 225 (18620), 274 (3240) and 280 (2880) nm. $^m/_z$ (NH_3, CI): 332 (MNH_4^+, 58), 315(MH^+, 94) and 105 (100).

Methyl 3-(4-methoxy-2-pivaloyloxyphenyl)propanoate (7g). Methyl 2'-pivaloyloxy-4'-methoxy cinnamate (**6g**) (1.84g, 6.31mmol) was dissolved in ethyl acetate (100ml) and 5% Pd-C (0.20g) was added cautiously to the solution. The mixture was stirred under hydrogen at ambient temperature and pressure for 1h when hydrogen uptake ceased. Flash chromatography (1:3 diethyl ether / pentane) afforded methyl 3-(4-methoxy-2-pivaloyloxyphenyl)propanoate (**7g**) (1.84g, quant.) as a colourless oil. (Found: C, 65.58%; H, 7.80%. $C_{16}H_{22}O_5$ requires: C, 65.29%; H, 7.53%). ^{1}HNMR ($CDCl_3$): δ 1.39 (9H, s), 2.55 (2H, t, J=8Hz), 2.78 (2H, t, J=8Hz), 3.66 (3H, s), 3.77 (3H, s), 6.55 (1H, d, J=2Hz), 6.73 (1H, dd, J=2.0, 8.5Hz) and 7.13 (1H, d, J=8.5Hz). υ_{max} ($CHCl_3$): 1805, 1738 and 1620 cm^{-1}. λ_{max} (EtOH): 202 (9550), 222 (7080), 273 (1550) and 280 (1350) nm. $^m/_z$ (NH_3, CI): 312 (MNH_4^+, 85), 295 (MH^+, 100), 210 (27), 178 (16) and 137 (14).

Methyl 3-(2-formyloxy-4-methoxyphenyl)propanoate (7h). Methyl 3-(2-hydroxy-4-methoxy phenyl)propanoate (**147**) (0.468g, 2.23mmol) was dissolved in pyridine under nitrogen at –10°C and formic acetic anhydride (0.392g, 4.46mmol) was added dropwise with stirring while maintaining the temperature below –5°C. The mixture was stirred at –5°C for 2h when no starting material was observed by TLC (1:1 diethyl ether / pentane). Removal of the solvent *in vacuo* followed by flash chromatography (1:1 diethyl ether / pentane) afforded methyl 3-(2-formyloxy-4-methoxyphenyl)propanoate (**7h**) (0.495g, 93%) as a colourless oil. (Found: C, 60.38%; H, 5.91%. $C_{12}H_{14}O_5$ requires: C, 60.50%; H, 5.92%). ^{1}HNMR ($CDCl_3$): δ 2.58 (2H, t, J=8Hz), 2.85 (2H, t, J=8Hz), 3.63 (3H, s), 3.80 (3H, s), 6.63 (1H, d, J=2.5Hz), 6.78 (1H, dd, J=2.5, 8.5Hz), 7.17 (1H, d, J=8.5Hz) and 8.32 (1H, s). υ_{max} ($CHCl_3$): 1735, 1620 and 1582 cm^{-1}. λ_{max} (EtOH): 204 (13180), 221 (4570), 278 (3390) and 282 (3310) nm. $^m/_z$ (IBEI): 238 (M^+, 7), 210 (27), 178 (81), 150 (48) and 137 (100).

General Method for Fries rearrangements: Methyl 3-(2-hydroxy-5-isovaleryl-4-methoxyphenyl)propanoate (8a). Methyl 3-(2-isovaleroyl-4-methoxyphenyl)propanoate (**7a**) (1.30g, 4.42mmol) was dissolved in nitromethane (15ml) and cooled to –10°C with stirring under nitrogen. A solution of anhydrous aluminium chloride (2.95g, 22.1mmol) in nitromethane (15ml) was added dropwise over 5 min and the mixture allowed to warm up to room temperature. Stirring was continued at room temperature for a further 0.5h when no starting material was observed by TLC (diethyl ether). The mixture was then quenched with ice-cold 5M hydrochloric acid (100ml), extracted with diethyl ether (150ml), and the organic extract washed with saturated sodium bicarbonate (2x30ml), washed with brine until neutral and dried over anhydrous magnesium sulphate. Complete removal of the solvent *in vacuo* below 40°C (***CAUTION!*** nitromethane may explode if heated[21]) followed by flash chromatography (1:2 diethylether / pentane) afforded methyl 3-(2-hydroxy-5-isovaleryl-4-methoxyphenyl)propanoate (**8a**) (0.84g, 65%) which was obtained from ethyl acetate / hexane as needles, mp 117-119°C. (Found: C, 65.33%; H, 7.53%. $C_{16}H_{22}O_5$ requires: C, 65.29%; H, 7.53%). ^{1}HNMR ($CDCl_3$): δ 0.94 (6H, d, J=7Hz), 2.21 (1H, m), 2.73 (2H, m), 2.83 (2H, d, J=7Hz), 2.85 (2H, m), 3.72 (3H, s), 3.86 (3H, s), 6.49 (1H, s), 7.57 (1H, s) and 8.35 (1H, s). υ_{max} ($CHCl_3$): 3280, 1708, 1654 and 1608 cm^{-1}. λ_{max} (EtOH): 203 (12020), 206(sh, 11750), 208(sh, 9550), 230, 9120) 268 (6310) and 308 (5010) nm. $^m/_z$ (NH_3, DCI): 295 (MH^+, 89), 263 (100), 237 (30), 220 (16), 205 (74), 191 (12), 177 (20) and 163 (13).

Methyl 3-(2-hydroxy-4-methoxy-5-senecioylphenyl)propanoate (8b). Prepared by the general method given above. Starting materials; methyl 3-(4-methoxy-2-senecioyloxyphenyl)propanoate (**7b**) (1.65g, 5.65mmol) in nitromethane (15ml), anhydrous aluminium chloride (3.92g, 29.5mmol) in nitromethane (15ml). Flash chromatography (3:1 diethyl ether / pentane) afforded methyl 3-(2-hydroxy-4-methoxy-5-senecioyl phenyl)propanoate (**8b**) (1.20g, 73%), obtained as needles from ethyl acetate / hexane, mp 115-116°C (Found: C, 65.71%; H, 6.98%. $C_{16}H_{20}O_5$ requires: C, 65.74%; H, 6.90%). ^{1}HNMR ($CDCl_3$): δ 1.96(3H, d, J=1Hz), 2.19 (3H, d, J=1Hz), 2.73 (2H, m), 2.85 (2H, m), 3.71 (3H, s), 3.81 (3H, s), 6.48 (1H, s), 6.69 (1H, m), 7.47 (1H, s) and 8.35 (1H, s). υ_{max} ($CHCl_3$): 3300, 1730 and 1640 cm^{-1}. λ_{max} (EtOH): 205 (11480), 230 (12880), 270 (8910) and 310 (14120) nm. $^m/_z$ (IBEI): 292 (M^+, 13), 274 (9), 259 (47), 245 (32), 229 (34), 217 (40), 205 (100), 201 (26), 187 (36) and 163 (24).

Methyl 3-(5-acetyl-2-hydroxy-4-methoxyphenyl)propanoate (8c). Prepared by the general method given above. Starting materials; methyl 3-(2-acetoxy-4-methoxyphenyl)propanoate (**7c**) (2.41g, 9.6mmol) in nitromethane (15ml), anhydrous aluminium chloride (6.37g, 47.8mmol) in nitromethane (20ml). Flash chromatography (1:1 diethyl ether / pentane) afforded firstly methyl 3-(5-acetyl-2-hydroxy-4-methoxyphenyl) propanoate (**8c**) (1.71g, 71%) and then a small amount of methyl 3-(5-acetyl-2,4-dihydroxyphenyl)propanoate (0.16g, 7%). Product (**8c**) was obtained from ethyl acetate / hexane as needles, mp 133-134°C. (Found: C,

61.77%; H, 6.57%. $C_{13}H_{16}O_5$ requires: C, 61.93%; H, 6.40%). ^{1}HNMR ($CDCl_3$): δ 2.58 (3H, s), 2.73 (2H, m), 2.85 (2H, m), 3.72 (3H, s), 3.86 (3H, s), 6.51 (1H, s), 7.64 (1H, s) and 8.45 (1H, s). υ_{max} ($CHCl_3$): 3278, 1710, 1656 and 1610 cm^{-1}. λ_{max} (EtOH): 210 (13800), 230 (14790), 268 (10000) and 310 (8320) nm. $^m/_z$ (EI) at m/e: 252 (M^+, 48), 205 (100), 179 (35), 177 (24) and 163 (14). Methyl 3-(5-acetyl-2,4-dihydroxyphenyl)propanoate was also recrystallised from ethyl acetate / hexane being obtained as needles, mp 141.5-143.5°C (Found: C, 60.57%; H, 6.03%. $C_{12}H_{14}O_5$ requires: C, 60.50%; H, 5.92%). ^{1}HNMR ($CDCl_3$): δ 2.55 (3H, s), 2.71 (2H, t, J=8Hz), 2.86 (2H, t, J=8Hz), 3.73 (3H, s), 6.41 (1H, s), 7.47 (1H, s), 7.96 (1H, bs) and 12.49 (1H, s). υ_{max} ($CHCl_3$): 1720 and 1636 cm^{-1}. λ_{max} (EtOH): 213 (10960), 232 (7080), 276 (8320) and 322 (4680) nm. $^m/_z$ (EI): 238 (M^+, 100), 223 (10), 206 (62), 191 (100), 178 (28), 163 (98) and 147 (23).

Methyl 3-(2-hydroxy-4-methoxy-5-propanoylphenyl)propanoate (8d). Prepared by the general method given above. Starting materials; methyl 3-(4-methoxy-2-propanoyloxyphenyl)propanoate (**7d**) (3.08g, 11.6mmol) in nitromethane (25ml), anhydrous aluminium chloride (7.71g, 57.9mmol) in nitromethane (25ml). Flash chromatography (1:1 diethyl ether / pentane afforded methyl 3-(2-hydroxy-4-methoxy-5-propanoylphenyl)propanoate (**8d**) (1.91g, 62%) obtained from ethyl acetate / hexane as needles, mp 106.5-107.5°C. (Found: C, 63,23%; H, 6.94%. $C_{14}H_{18}O_5$ requires: C, 63.15%; H, 6.81%). ^{1}HNMR ($CDCl_3$): δ 1.15 (3H, t, J=7Hz), 2.73 (2H, m), 2.87 (2H, m), 2.97 (2H, q, J=7Hz), 3.71 (3H, s), 3.84 (3H, s), 6.50 (1H, s), 7.62 (1H, s) and 8.42 (1H, s). υ_{max} ($CHCl_3$): 3280, 1709, 1660 and 1610 cm^{-1}. λ_{max} (EtOH): 210 (12020), 230 (12590), 267 (8510) and 307 (6760) nm. $^m/_z$ (IBEI): 266 (M^+, 11), 236 (21), 234 (22), 205 (100), 177 (41), 163 (26) and 151 (9).

Methyl 3-(2-hydroxy-5-isobutanoyl-4-methoxyphenyl)propanoate (8e). Prepared by the general method given above. Starting materials; methyl 3-(2-isobutanoyloxy-4-methoxyphenyl)propanoate (**7e**) (1.08g, 3.96mmol) in nitromethane (15ml), anhydrous aluminium chloride (2.64g, 20mmol) in nitromethane (15ml). Flash chromatography (1:1 diethyl ether / pentane) afforded methyl 3-(2-hydroxy-5-isobutanoyl-4-methoxyphenyl)propanoate (**8e**) (0.39g, 35%), obtained from ethyl acetate / hexane as needles, mp 129-130.5°. (Found: C, 64.56%; H, 7.35%. $C_{15}H_{20}O_5$ requires: C, 64.27%; H, 7.19%). ^{1}HNMR ($CDCl_3$): δ 1.13 (6H, d, J=7Hz), 2.73 (2H, t, J=4Hz), 2.85 (2H, t, J=4Hz), 3.56 (1H, q, J=7Hz), 3.71 (3H, s), 3.84 (3H, s), 6.50 (1H, s), 7.50 (1H, s) and 8.33 (1H, bs). υ_{max} ($CHCl_3$): 3280, 1710, 1660, 1610 and 1573 cm^{-1}. λ_{max} (EtOH): 211 (11750), 230 (12020), 268 (7940) and 307 (6310) nm. $^m/_z$ (NH_3, DCI): 281 (MH^+, 84), 249 (81), 237 (32), 205 (100) and 177 (14).

Methyl 3-(5-benzoyl-2-hydroxy-4-methoxyphenyl)propanoate (**8f**). Prepared by the general method given above. Starting materials; methyl 3-(2-benzoyloxy-4-methoxyphenyl)propanoate (**7f**) 1.23g, 3.89mmol) in nitromethane (15ml), anhydrous aluminium chloride (2.60g, 19.46mmol) in nitromethane (15ml). Flash chromatography (1:1 diethyl ether / pentane) afforded methyl 3-(2-benzoyloxy-4-methoxyphenyl)propanoate (**8f**) (0.21g, 17%) which was recrystallised from ethyl acetate / hexane as needles, mp 147-148.5°C. (Found: C, 68.84%; H, 5.82%. $C_{18}H_{18}O_5$ requires: C, 68.78%; H, 5.77%). ^{1}HNMR ($CDCl_3$): δ 3.67 (2H, m), 3.64 (3H, s), 3.73 (3H, s), 3.87 (2H, m), 6.54 (1H, s), 7.20 (1H, s), 7.40 (2H, t, J=5Hz), 7.52 (1H, t, J=5Hz), 7.77 (2H, d, J=5Hz) and 8.28 (1H, bs). υ_{max} ($CHCl_3$): 3280, 1710, 1648, 1612 and 1579 cm^{-1}. λ_{max} (EtOH): 205 (26920), 256 (14450), 281 (5250) and 319 (5250) nm. $^m/_z$ (NH_3, DCI): 315 (MH^+, 100), 283 (90), 205 (14) and 105 (19).

3,4-Dihydro-6-isovaleryl-7-methoxycoumarin (10a). Methyl 3-(5-isovaleryl-2-hydroxy-4-methoxyphenyl)propanoate (**8a**) (0.50g, 1.7mmol) was dissolved in diphenyl ether (5ml) at 30°C and the solution refluxed for 3h under nitrogen. After cooling, the residue was subjected to flash chromatography (1:4 diethyl ether / pentane) which afforded 3,4-dihydro-6-isovaleryl-7-methoxycoumarin (**10a**) (0.257g, 58%). Recrystallisation from ethyl acetate / hexane gave needles, mp 86.5-87.5°C. (Found: C, 68.99%; H, 7.10%. $C_{15}H_{18}O_4$ requires: C, 68.69%; H, 6.92%). ^{1}HNMR ($CDCl_3$): δ 0.90 (6H, d, J=7Hz), 2.10 (1H, m), 2.70 (2H, d, J=7Hz), 2.76 (4H, m), 3.83 (3H, s), 6.66 (1H, s), 7.62 (1H, s). υ_{max} ($CHCl_3$): 1774, 1735, 1670, 1618 and 1582 cm^{-1}. λ_{max} (EtOH): 208(sh, 13490), 216 (15140), 254 (7410) and 304 (4070) nm. $^m/_z$ (EI): 262 (M^+, 13), 220 (11), 205 (100), 203 (18), 177 (32) and 163 (21).

3,4-dihydro-7-methoxy-6-senecioylcoumarin (10b). Rearrangement product (**8b**) (0.10g, 0.34mmol) was dissolved in diphenyl ether (5ml) at 30°C and refluxed under nitrogen for 3h. After cooling, flash chromatography (1:6 diethyl ether / pentane) afforded 3,4-dihydro-7-methoxy-6-senecioylcoumarin (**10b**) (0.075g, 84%) which was recrystallised from ethyl acetate / hexane to give needles, mp 94-95°C. (Found: C, 69.11%; H, 6.24%. $C_{15}H_{16}O_4$ requires: C, 69.22%; H, 6.20%). ^{1}HNMR ($CDCl_3$): δ 1.93 (3H, s), 2.10 (3H, s), 2.80 (4H, m), 3.77 (3H, s), 6.57 (2H, m), 7.40 (1H, s). υ_{max} ($CHCl_3$): 1735 and 1650 cm^{-1}. λ_{max}

(EtOH): 203 (13800), 225 (7080), 260 (9550) and 308 (10230) nm. $^{m}/_{z}$ (IBEI): 260 (M^+, 38), 259 (62), 245 (23), 229 (22), 217 (43) 205 (100), 201 (37), 187 (41), 177 (64) and 163 (46).

3,4-Dihydro-7-methoxy-6-propanoylcoumarin (10d). Methyl 3-(2-hydroxy-4-methoxy-5-propanoyl)propanoate (**8d**) (0.41g, 1.55mmol) was refluxed in diphenyl ether (5ml) under nitrogen for 3h. Flash chromatography (1:4 diethyl ether / pentane afforded 3,4-dihydro-7-methoxy-6-propanoylcoumarin (**10d**) (0.30g, 83%) which was recrystallised from ethyl acetate / hexane to give needles, mp 109-110°C. (Found: C, 67.05%; H, 6.23%. $C_{13}H_{14}O_4$ requires: C, 66.66%; H, 6.02%). ^{1}HNMR ($CDCl_3$): δ 1.16 (3H, s), 2.80 (2H, t, J=8Hz), 2.98 (4H, m), 3.89 (3H, s), 6.65 (1H, s) and 7.64 (1H, s). υ_{max} ($CHCl_3$): 1772, 1670 and 1608 cm^{-1}. λ_{max} (EtOH): 214 (18620), 254 (8910) and 300 (3980) nm. $^{m}/_{z}$ (NH_3, CI): 235 (MH^+, 100) and 205 (21).

Geijerin (6-isovaleryl-7-methoxycoumarin) (4a). Methyl 3-(2-hydroxy-5-isovaleryl-4-methoxy phenyl)propanoate (**8a**) (0.067g, 0.23mmol) was dissolved in diphenyl ether (5ml) at 30°C and 5% Pd-C (0.067g) was added. The mixture was refluxed under nitrogen for 3h when no starting material was observed by TLC (diethyl ether). After cooling, hot ethanol was added and the solution filtered through a 2 cm pad of Celite®. Removal of solvent *in vacuo* followed by flash chromatography (initially 1:9 diethyl ether / pentane to remove Ph_2O, followed by 1:2 diethyl ether / pentane) afforded geijerin (**4a**) (0.039g, 66%) which was recrystallised from ethyl acetate / hexane to give needles, mp 122-122.5°C (lit.[14] 121°C). ^{1}HNMR ($CDCl_3$): δ 0.95 (6H, d, J=7Hz), 2.22 (1H, m), 2.85 (2H, d, J=7Hz), 3.98 (3H, s), 6.30 (1H, d, J=9.5Hz), 6.85 (1H, s), 7.67 (1H, d, J=9.5Hz) and 7.83 (1H, s). υ_{max} ($CHCl_3$): 1750 and 1680 cm^{-1}. λ_{max} (EtOH): 215 (sh, 10230), 220(15850), 255 (14130), 310 (7240) and 317 (10470) nm. $^{m}/_{z}$ (IBEI): 260 (M^+, 15) and 155 (19).

Dehydrogeijerin (7-methoxy-6-senecioylcoumarin) (4b). 3,4-Dihydro-7-methoxy-6-senecioyl-coumarin (**10b**) (0.095g, 0.36mmol) was dissolved in diphenyl ether at 30°C and 5% Pd-C (0.10g) was added, together with 1-dodecene (1ml) as a hydrogen acceptor. The mixture was refluxed under nitrogen for 3h when no starting material was observed by TLC (diethyl ether). After cooling, hot ethanol was added and the solution filtered through a 2 cm pad of Celite®. Removal of solvent *in vacuo* followed by flash chromatography (initially 1:9 diethyl ether / pentane to remove Ph_2O, followed by 1:1 diethyl ether / pentane) afforded dehydrogeijerin (**4b**) (0.009g, 10%) which was recrystallised from ethyl acetate / hexane to give needles, mp 125-128°C (lit.[15] 130-131°C). ^{1}HNMR ($CDCl_3$): δ 2.00 (3H, d, J=1.2Hz), 2.24 (3H, d, J=1.2Hz), 3.95 (3H, s), 6.30 (1H, d, J=9.5Hz), 6.62 (1H, m), 6.84 (1H, s), 7.67 (1H, d, J= 9.5Hz) and 7.73 (1H, s). υ_{max} ($CHCl_3$): 1725 and 1670 cm^{-1}. λ_{max} (EtOH): 202 (15490), 226 (9120), 255 (10000) and 318 (10000) nm. *m/z* (IBEI): 258 (M^+, 30), 243 (12), 175 (100).

6-Acetyl-7-methoxycoumarin (4c). Methyl 3-(5-acetyl-2-hydroxy-4-methoxyphenyl)propanoate (**8c**) (0.41g, 1.6mmol) was dissolved in diphenyl ether (5ml) at 30°C and 5% Pd-C (0.41g) was added. The mixture was refluxed under nitrogen for 3h when no starting material was observed by TLC (diethyl ether). After cooling, hot ethanol was added and the solution filtered through a 2 cm pad of Celite®. Removal of the solvent *in vacuo* followed by flash chromatography (initially 1:9 diethyl ether/ pentane to remove Ph_2O, followed by 1:1 diethyl ether / pentane) afforded 6-acetyl-7-methoxycoumarin (**4c**) (0.25g, 70%), obtained as needles from ethyl acetate / hexane, mp 180-182°C. (Found: C, 65.83%; H, 4.58%. $C_{12}H_{10}O_4$ requires: C, 66.05%; H, 4.62%). ^{1}HNMR ($CDCl_3$): δ 2,64 (3H, s), 4.01 (3H, s), 6.32 (1H, d, J=9.5Hz), 6.88 (1H, s), 7.68 (1H, d, J=9.5Hz) and 7.96 (1H, s). υ_{max} ($CHCl_3$): 1732, 1680, 1617 and 1600 cm^{-1}. λ_{max} (EtOH): 214 (11750), 219(sh, 11220), 225(sh, 10230), 250 (14790), 304 (7940) and 324 (9120) nm. $^{m}/_{z}$ (IBEI): 218 (M^+, 25), 175 (26) and 160 (15).

7-Methoxy-6-propanoylcoumarin (4d). Prepared by the method given above for geijerin (**4a**). Starting materials; methyl 3-(2-hydroxy-4-methoxy-5-propanoylphenyl)propanoate (**8d**) (0.437g, 1.64mmol) in diphenyl ether (5ml) and 5% Pd-C (0.437g). Flash chromatography (1:4 diethylether / pentane) afforded 7-methoxy-6-propanoylcoumarin (**4d**) (0.190g, 50%) and a small amount of 7-hydroxy-6-propanoylcoumarin (0.031g, 9%). Product (**4d**) was recrystallised from ethyl acetate / hexane giving needles, mp 175-176°C. (Found: C, 67.39%; H, 5.23%. $C_{13}H_{12}O_4$ requires: C, 67.23%; H, 5.21%). ^{1}HNMR ($CDCl_3$): δ 1.18 (3H, t, J=7.2Hz), 3.01 (2H, q, J=7.2Hz), 3.99 (3H, s), 6.32 (1H, d, J=9.5Hz), 6.87 (1H, s), 7.68 (1H, d, J=9.5Hz) and 7.91 (1H, s). υ_{max} ($CHCl_3$): 1734, 1665, 1618 and 1606 cm^{-1}. λ_{max} (EtOH): 214 (13490), 249 (15850), 302 (9120) and 322 (10470) nm. $^{m}/_{z}$ (EI): 232 (M^+, 20), 203 (100), 175 (16) and 160 (15). 7-Hydroxy-6-propanoylcoumarin was also recrystallised from ethyl acetate / hexane and was obtained as needles, mp 159-160°C. (Found: C, 66.14%; H, 4.58%. $C_{12}H_{10}O_4$ requires: C, 66.05%; H, 4.62%). ^{1}HNMR ($CDCl_3$): δ 1.29(3H, t, J=7.3Hz), 3.09 (2H, q, J=7.3Hz), 6.30 (1H, d, J=9.5Hz), 6.88 (1H, s), 7.64 (1H, d, J=9.5Hz), 7.93 (1H, s) and 12.78 (1H, s). υ_{max} (KBr disc, FTIR): 3451, 1741, 1645 and 1573 cm^{-1}. λ_{max}

(EtOH): 205 (6170), 226 (7590), 254 (14450), 301(sh, 5130), 308 (5500) and 338 (6030) nm. $^{m}/_{z}$ (EI): 218 (M^+, 38), 189 (100), 161 (22), 133 (10) and 105 (17).

6-Isobutanoyl-7-methoxycoumarin (4e). Prepared by the method given above for geijerin (**4a**). Starting materials; methyl 3-(2-hydroxy-5-isobutanoyl-4-methoxyphenyl)propanoate (**8e**) (0.18g, 0.643mmol) in diphenyl ether (5ml), 5% Pd-C (0.18g), reflux time 4h. Flash chromatography (1:1 diethyl ether / pentane) afforded (**4e**) (0.85g, 54%) which was recrystallised from ethyl acetate / hexane to give needles, mp 115-117°C. (Found: C, 68.10%; H, 5.74%. $C_{14}H_{14}O_4$ requires: C, 68.28%; H, 5.73%). ^{1}HNMR ($CDCl_3$): δ 1.60 (6H, d, J=7Hz), 3.50 (1H, qn, J=7Hz), 3.97 (3H, s), 6.31 (1H, d, J=9.5Hz), 6.86 (1H, s), 7.67 (1H, d, J=9.5Hz) and 7.73 (1H, s). υ_{max} (KBr disc, FTIR): 1742, 1731, 1678, 1663 and 1616 cm^{-1}. λ_{max} (EtOH): 209 (13490), 214 (sh, 13180), 246 (14120), 304 (9330) and 318 (10960) nm. $^{m}/_{z}$ (EI): 246 (M^+, 7), 203 (100), 175 (9) and 160 (7).

6-Benzoyl-7-methoxycoumarin (4f). Prepared by the method given above for geijerin (**4a**). Starting materials; methyl 3-(5-benzoyl-2-hydroxy-4-methoxyphenyl)propanoate (**8f**) (0.03g, 0.96mmol) in diphenyl ether (5ml) 5% Pd-C (0.03g), reflux time 5h. Flash chromatography (1:1 diethyl ether / pentane) afforded (**4g**) (0.017g, 64%) which was recrystallised from ethyl acetate / hexane and obtained as needles, mp 142-144°C. (Found: C, 72.58%; H, 4.38%. $C_{17}H_{12}O_4$ requires: C, 72.85%; H, 4.32%). ^{1}HNMR ($CDCl_3$): δ 3.82 (3H, s), 6.33 (1H, d, J=9Hz), 6.92 (1H, s), 7.37 (2H, t, J=6Hz), 7.53 (1H, s), 7.68 (1H, t, J=5Hz), 7.69 (1H, d, J=9Hz) and 7.80 (2H, d, J=6Hz). υ_{max} ($CHCl_3$): 1710 and 1640 cm^{-1}. λ_{max} (EtOH): 210 (12590), 259 (16980), 310 (7940) and 325 (10000) nm. $^{m}/_{z}$ (NH_3, CI): 281 (MH^+, 100%), 203 (12) and 105 (9).

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