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CLAISEN REARRANGEMENTS—XV

STRUCTURE REVISION OF THE COUMARIN, CELERIN, BY SYNTHESIS

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Abstract—The four possible structures, **9**, **12**, **17** and **26** for celerin have been synthesised and the structure of the natural product revised to 8-hydroxy-7-methoxy-5-(1,1-dimethylallyl)coumarin **26**. Efficient alternative synthetic routes to sibiricol **5**, coumurrayin **6** and pinnarin **13** have been established.

Studies by Garg, Gupta and Sharma of the seed constituents of *Apium graveolens* (Umbelliferae) have revealed the presence of thirteen coumarins.[2-6] Apart from celerin,[2] m.p. 154–156°, three of these are 7-oxygenated coumarins—umbelliferone,[3] osthenol[3] and seselin;[3] three are 5,7-dioxygenated-bergapten,[3] isoimperatorin[3] and celereoside;[4] four are 7,8-dioxygenated-apigravin[3] (7-hydroxy-8-methoxy-6-prenylcoumarin), apiumetin,[5] rutaretin[5] and apiumoside;[6] while two have a 5,7,8-trioxygenated nucleus—8-hydroxybergapten[3] and isopimpinellin.[3] Celerin was deduced to be 6-hydroxy-7-methoxy-8-(1,1-dimethylallyl)coumarin **1**[2] but recent synthetic studies in our laboratory revealed[7] that celerin is neither of the monomethyl ethers of obliquetol [6,7-dihydroxy-8-(1,1-dimethylallyl)-coumarin].

Biogenetic considerations[8] require that celerin possesses an oxygen substituent at C-7. The possibility of this being OH was precluded from the absence of a bathochromic shift in the UV maxima of celerin on addition of sodium acetate.[2,8] However, the Indian workers report[2] of a bathochromic shift in the UV maxima of demethylated celerin, on addition of sodium acetate, is consistent with the presence of a 7-OMe group in the natural product.

The ^{1}H NMR signals reported[2] for celerin reveal the H-4 doublet to be centred at δ 8.28. The normal range for H-4 (in $CDCl_3$) for coumarins is δ 7.5–7.9[8,9] and only when C-5 carries an alkyl, OH or alkoxyl substituent does the H-4 resonance shift downfield to δ 7.9–8.2.[8-10] Consequently celerin must have either the OH or the 1,1-dimethylallyl unit at C-5 and thus four structures must be considered for the natural product, two with the OH at C-5 and the 1,1-dimethylallyl group at C-6 or C-8, **9** and **12**, and conversely two with the alkenyl residue at C-5 and the OH at C-6 or C-8, **17** and **26**. The synthesis of each of these compounds is reported herein.

The two 5,7-dioxygenated coumarins **9** and **12** were obtained as follows. In 1975, we discovered[11] that 5-prenyloxy-7-methoxycoumarin **2** underwent exclusive *para*-Claisen rearrangement on heating in butyric anhydride/diethylaniline giving the butyrate **3** despite the availability of an *ortho* position for rearrangement. Recently we found[12] that the problem of freeing products from traces of reagents, attendant on such reactions, could be circumvented by using acetic anhydride and omitting the amine. Thus 5-prenyloxy-7-acetoxycoumarin in refluxing anhydride gave the *para*-Claisen rearrangement product, 5,7-diacetoxy-8-prenylcoumarin.[13] When 5-prenyloxy-7-methoxycoumarin **2** was treated in the same way, the anticipated *para* rearrangement to the acetate **4** occurred, again in quantitative yield. Deacetylation of **4** using the mild conditions of Zn dust in MeOH[14] gave the corresponding phenol, sibiricol **5**,[15] the penultimate product in our previous synthesis of coumurrayin **6**.[16] However, overnight exposure of **4** to ten equivalents of 1% methanolic NaOH afforded an equilibrium mixture (85 : 14) of sibiricol and the 5-hydroxycoumarin **7** from lactone-ring isomerisation.[12] Although the yield of the latter phenol is low, the two products can readily be separated by chromatography thereby providing an alternative synthetic route to toddaculin **8**.[11]

We envisaged that **9** could be obtained by a Claisen rearrangement of **2** if the intermediate *ortho*-dienone[11] could be induced to enolise instead of undergoing the further sigmatropic shift to the *para* position. In our recent synthesis of hortiolone,[12] the combination of acetic anhydride and sodium acetate was utilised to prevent incursion of a rapid abnormal Claisen rearrangement. Under these conditions, **2** afforded the acetate **10** of the desired *ortho*-rearrangement product in 86% yield although *para* rearrangement to **4** (11%) could not be totally excluded. The structure of **10** followed from its ^{1}H NMR spectrum which disclosed signals for a 1,1-dimethylallyl unit and long-range coupling of H-4 with H-8, requiring the alkenyl substituent to be located at C-6.[17] The acetate **10** was inert to attempted deacetylation with Zn dust in MeOH but after treatment with one equivalent of 0.5% methanolic NaOH for 4 hr, a mixture was obtained of the desired phenol **9** (75%), m.p. 105–107°, the isomer **12** (6%), m.p. 175–177° resulting from lactone-ring isomerisation[11] and residual starting material (9%). An equilibrium mixture of **12** (91%) having the 1,1-dimethylallyl group at C-8 and **9** (9%), where this bulky group is at C-6, was obtained after 12 hr treatment of **10** with ten equivalents 3% methanolic NaOH. The melting points of these two 5-hydroxycoumarins indicate that neither can be celerin, as do their ^{1}H NMR spectra. Their singlet aromatic protons resonate at δ 6.52 and 6.47, respectively, compared with δ 7.03 for celerin, while the H-4 doublets are centred at δ 8.05 and 7.98, respectively. Confirmation of the structure **12** of the phenol obtained after lactone-ring isomerisation came from methylation, which gave pinnarin **13**.[18] It should be noted that in both syntheses of this natural

coumarin, the nuclear 1,1-dimethylallyl group is introduced by a prenyl ether *ortho*-Claisen rearrangement, in our first synthesis[18] directly to C-8 from 5-methoxy-7-prenyloxycoumarin and now indirectly from the positional isomer **2**.

The two OMe resonances of pinnarin at δ 3.84 and 3.93 are close to those of 5,7-dimethoxycoumarin (δ 3.83 and 3.88)[19] whereas the OMe signals for **11** resonate at δ 3.83 and 3.65. The last value is at higher field than normally found[19] for methoxycoumarins (δ 3.8–4.4) and implies that one of the OMe groups, presumably that at C-5, adopts an out-of-plane conformation[20] due to the proximity of the bulky 1,1-dimethylallyl group at C-6 and the *peri* hydrogen at C-4. In contrast the OMe signals for toddaculin **8**[11] the isomer of **11** having a 3,3-dimethylallyl, instead of a 1,1-dimethylallyl, group at C-6, resonate at δ 3.82 and 3.86.

The third possibility **17** for celerin, which again contains a 1,1-dimethylallyl group *ortho* to a phenol, was obtained by the first example of an *ortho*-Claisen rearrangement of a 6-allyloxycoumarin. The major product **18** (80%) from heating 6-prenyloxy-7-methoxycoumarin **15** in acetic anhydride containing sodium acetate was accompanied however by the acetate **16** (14%) from prenyl ether cleavage, a known alternative reaction pathway.[21]

The acetate **18** was inert to Zn dust in MeOH, a deacetylation process which we have found to be ineffective for hindered acetates. Complete hydrolysis of **18** required eight equivalents of 2% methanolic NaOH for 8 hr but the desired phenol **17** (65%) m.p. 92–94° was accompanied by the 2,3,3-trimethyldihydrofuranocoumarin **20** (31%). Treatment of **18** with a vast excess (150 equivalents) of 10% methanolic NaOH for 10 min gave the phenol **17** (97%) uncontaminated with the cyclic isomer. The ^{1}H NMR spectrum of **17** is close to that reported[2] for celerin with H-4 centred at δ 8.30 and the benzenoid proton at δ 6.73, but the difference of 62° in m.ps precludes this possibility for the natural coumarin. Moreover, there is no indication[2] that solutions of celerin are unstable whereas **17** was readily converted to the dihydrofuran **20** on standing in $CHCl_3$ or ethyl acetate at room temperature.

We envisaged that the final possibility, **26**, for celerin could be obtained by the *para*-Claisen rearrangement[1] of the 1,1-dimethylallyl ether **24**. The requisite phenol, 8-hydroxy-7-methoxycoumarin **21** was conveniently obtained by the known[22] selective demethylation of 7,8-dimethoxycoumarin **22** in sulphuric acid at 70°. Extending the reaction time from the recommended 14 hr to 6 days however has resulted in a yield improvement from 29 to 77%.

The phenol **21** was completely inert to 3-chloro-3-methylbut-1-yne using the normal etherification conditions[11,23] and even prolonged exposure to potassium carbonate and potassium iodide in moist acetone in a closed system, used in the synthesis of benahorin,[1] gave the desired ether **23** in only 15% yield, the *C,O*-dialkylated product **29** (4%) but mainly unreacted starting material. However, in the presence of cesium carbonate and dry acetone in a closed system, **21** reacted completely after 36 hr to give the ether **23** (46%) and a number of by-products, though not **29**, which are currently being investigated.

Partial hydrogenation of **23** over 5% Pd–$BaSO_4$ followed by chromatography gave the tetrahydro compound **25** (17%) and the required 1,1-dimethylallyl ether **24** (71%) which quantitatively underwent a *para*-Claisen rearrangement in acetic anhydride and sodium acetate giving **27**. Hydrolysis of **27** with 1% methanolic NaOH gave the phenol **26**, m.p. 158–159.5°. This melting point is only 4° higher than that reported[2] for celerin while the ^{1}H NMR signals of **26** are similar to the published values for celerin except that those for the synthetic product are upfield by ~0.1 ppm. In particular, H-4 is centred at δ 8.22 and the aromatic H-6 proton at δ 6.93. The mass spectra of celerin and **26** *each* show a parent molecular ion and important fragmentation ions at *m/z* 245 and 213 with two consecutive losses of CO from the latter. The loss of 42 mass units (MeOH) from the first fragment ion in both spectra is quite unique for methoxycoumarins.[8] Although no sample of the natural product is available, direct comparison of the ^{1}H NMR and mass spectra of celerin (kindly provided by Prof. Gupta) and **26** has revealed their probable identity. In support of structure **26**, it should be noted that the reported[2] demethylation of celerin with pyridinium bromide to a diphenol followed by methylation to celerin methyl ether precludes the 1,1-dimethylallyl group being *ortho* to *either* oxygen function since cyclisation to a dihydrofuran would otherwise have undoubtedly occurred in the strongly acidic demethylation conditions.[8]

Apart from 5-methylcoumarins, only eight C-5 alkylated coumarins are known[8] all of which possess a 7,8-dioxygenated coumarin nucleus as significantly do four of the *A. graveolens* coumarins. Our results suggest that celerin should be reformulated as 8-hydroxy-7-methoxy-5-(1,1-dimethylallyl)coumarin **26**, the second example of a coumarin with a 1,1-dimethylallyl group at C-5, benahorin being the first.[1]

EXPERIMENTAL

For general experimental see preceding paper.

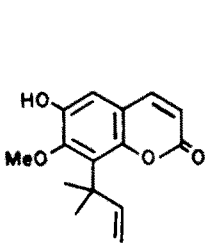
Claisen rearrangements of **2**

(i) A soln of **2** (80 mg) in Ac_2O (10 ml) was refluxed for 20 hr. Evaporation of the solvent under reduced pressure gave *5-acetoxy-7-methoxy-8-(3-methylbut-2-enyl)coumarin* **4** (92 mg, 100%) colourless needles, m.p. 120–121° (lit.[15] 124–125°) (from ether). (Found: C, 67.65; H, 6.0. $C_{17}H_{18}O_5$ requires: C, 67.55; H, 6.0%); ν_{max} 1770, 1730, 1612, 1565 and 1495 cm^{-1}; NMR signals at δ 1.63 (3H, bs), 1.81 (3H, bs), 2.35 (3H, s), 3.50 (2H, bd, *J* 7.5 Hz), 3.87 (3H, s), 5.2 (1H, bt, *J* 7.5 Hz), 6.22 (1H, d, *J* 9.5 Hz), 6.65 (1H, s) and 7.59 (1H, d, *J* 9.5 Hz).

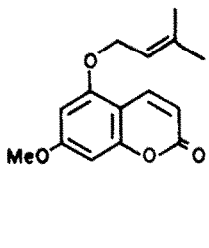
(ii) A mixture of **2** (228 mg), NaOAc (1.53 g) and Ac_2O (15 ml) was refluxed with stirring for 20 hr. The residue from filtration and evaporation was chromatographed on silica gel G. Elution with EtOAc–light petroleum (1:4) gave *5-acetoxy-7-methoxy-8-(1,1-dimethylallyl)coumarin* **10** (227 mg, 86%) colourless plates, m.p. 144–145° (from ether). (Found: C, 67.3; H, 6.2. $C_{17}H_{18}O_5$ requires: C, 67.55; H, 6.0%); ν_{max} 1770, 1730, 1620, 1610 and 1560 cm^{-1}; NMR signals at δ 1.48 (6H, s), 2.29 (3H, s), 3.89 (3H, s), 4.88 (1H, dd, *J* 10 and 2 Hz), 4.92 (1H, dd, *J* 17.5 and 2 Hz), 6.23 (1H, d, *J* 9.5 Hz), 6.27 (1H, dd, *J* 17.5 and 10 Hz), 6.74 (1H, s) and 7.43 (1H, d, *J* 9.5 Hz); and **4** (30 mg, 11%).

Hydrolysis of **4**

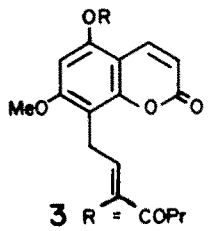
(i) A soln of **4** (13.5 mg) in MeOH (5 ml) was stirred with activated Zn[14] (from Zn dust, 150 mg) for 12 hr. After filtration through celite and washing with MeOH, the combined filtrates were evaporated under reduced pressure. The residue was partitioned between EtOAc and dil HCl,



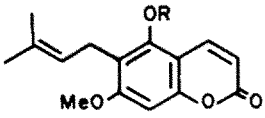
1



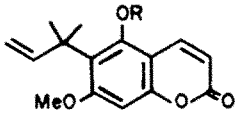
2



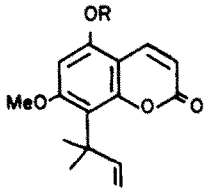
3 R = COPr
4 R = Ac
5 R = H
6 R = Me



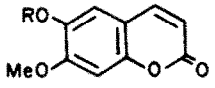
7 R = H
8 R = Me



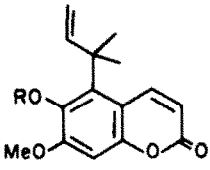
9 R = H
10 R = Ac
11 R = Me



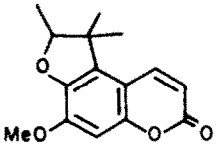
12 R = H
13 R = Me



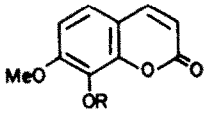
14 R = H
15 R = $CH_2CH{=}CMe_2$
16 R = Ac



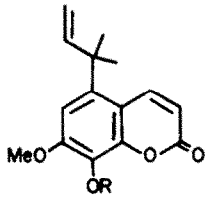
17 R = H
18 R = Ac
19 R = Me



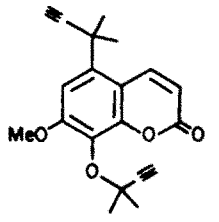
20



21 R = H
22 R = Me
23 R = $CMe_2C{\equiv}CH$
24 R = $CMe_2CH{=}CH_2$
25 R = CMe_2CH_2Me



26 R = H
27 R = Ac
28 R = Me



29

the organic layer washed with dil HCl, brine, dried and evaporated to give sibiricol **5** (11.5 mg 100%) colourless needles, m.p. 195–197° (lit.[15,16] 193–194°) (from EtOAc–light petroleum) identical (mmp, NMR and TLC) with an authentic sample.

(ii) A soln of **4** (56 mg, 0.185 mmole) in MeOH (5 ml) and 1% NaOH/MeOH (7.5 ml, 1.87 mmole) was stirred for 24 hr. After careful neutralisation with dil HCl, the solvent was evaporated and the residue partitioned between EtOAc and brine, the organic layer washed with brine, dried and evaporated. The residue was chromatographed on silica gel G. Elution with EtOAc–light petroleum afforded **7** (7 mg, 14%) colourless needles, m.p. 151–153° (lit.[11] 150–153°) (from EtOAc–light petroleum) identical (mmp, NMR and TLC) with an authentic sample; and **5** (41 mg, 85%).

Hydrolysis of **10**

(i) A soln of **10** (55 mg, 0.182 mmole) in MeOH (10 ml) and 0.5% NaOH/MeOH (1.42 ml, 0.182 mmole) was stirred for 4 hr until TLC disclosed maximal concentration of a less

polar product. Work up as for **7** followed by chromatography on silica gel G and elution with EtOAc–light petroleum (1:4) gave 5 - *hydroxy* - 7 - *methoxy* - 6 - (1,1 - *dimethylallyl*)*coumarin* **9** (35 mg, 75%) tan–yellow plates, m.p. 105–107° (from MeOH). (Found: C, 69.25; H, 6.1. $C_{15}H_{16}O_4$ requires: C, 69.2; H, 6.2%); ν_{max} 3410, 1775, 1620, 1610 and 1570 cm^{-1}; NMR signals at δ 1.55 (6H, s), 3.90 (3H, s), 5.45 (1H, dd, *J* 10 and 2 Hz); 5.53 (1H, dd, *J* 17.5 and 2 Hz), 6.17 (1H, d, *J* 9.5 Hz), 6.47 (1H, s), 6.53 (1H, dd, *J* 17.5 and 10 Hz), 7.40 (1H, s, OH) and 7.98 (1H, d, *J* 9.5 Hz); **10** (5 mg, 9%) and **12** (3 mg, 6%).

(ii) A soln of **10** (51 mg, 0.169 mmole) in MeOH (10 ml) and 3% NaOH/MeOH (2 ml, 1.5 mmole) was stirred overnight. Work up and chromatography as above gave **9** (4 mg, 9%) and 5 - *hydroxy* - 7 - *methoxy* - 8 - (1,1 - *dimethylallyl*)*coumarin* **12** (40 mg, 91%) colourless plates, m.p. 175–177° (from EtOAc–light petroleum). (Found: C, 69.5; H, 6.1. $C_{15}H_{16}O_4$ requires: C, 69.2; H, 6.2%); ν_{max} (KBr) 3300 (b), 1690, 1640 and 1575 cm^{-1}; NMR signals (acetone-d_6) at δ 1.61 (6H, s), 3.80 (3H, s), 4.79 (1H, dd, *J* 10 and 2 Hz), 4.83 (1H, dd, *J* 17.5 and 2 Hz), 6.06 (1H, d, *J* 9.5 Hz), 6.27 (1H, dd, *J* 17.5 and 2 Hz), 6.52 (1H, s) and 8.05 (1H, d, *J* 9.5 Hz).

Methylation of **9**

A mixture of **9** (16 mg), MeI (0.5 ml), K_2CO_3 (100 mg) and acetone (10 ml) was refluxed with stirring for 1 hr. The cooled mixture was filtered, the solvent evaporated and the residue partitioned between EtOAc and brine. The organic layer was washed with satd. aq. $NaHCO_3$, brine, dried and evaporated to give 5,7 - *dimethoxy* - 6 - (1,1 - *dimethylallyl*)*coumarin* **11** (17 mg) colourless needles, m.p. 88–90° (from ether–light petroleum). (Found: C, 69.45; H, 6.40. $C_{16}H_{18}O_4$ requires: C, 70.05; H, 6.6%); ν_{max} 1725, 1640, 1612, 1600 and 1565 cm^{-1}; NMR signals at δ 1.51 (6H, s), 3.65 (2H, s), 3.85 (3H, s), 4.82 (1H, dd, *J* 10 and 2 Hz), 4.87 (1H, dd, *J* 17.5 and 2 Hz), 6.24 (1H, d, *J* 9.5 Hz), 6.35 (1H, dd, *J* 17.5 and 10 Hz), 6.63 (1H, s) and 7.85 (1H, d, *J* 9.5 Hz).

Pinnarin **13**

Methylation of **12** (24 mg) as above gave pinnarin **13** (25.5 mg) colourless plates, m.p. 170–172° (lit.[24] 162–163°; lit.[18] 166–167°) (from ether). (Found for natural sample[24] 170–172°—found for synthetic sample[18] 169–171°) identical (mmp, NMR, IR and TLC) with authentic samples.

Synthesis and Claisen rearrangement of **15**

A mixture of **14**[25] (514 mg), K_2CO_3 (1.45 g), prenyl bromide (540 mg) and acetone (50 ml) was refluxed for 1 hr. Work up as for **11** gave 6 - (3 - *methylbut* - 2 - *enyloxy*) - 7 - *methoxycoumarin* **15** (680 mg, 98%) colourless plates, m.p. 116–118° (from EtOAc–hexane). (Found: C, 69.5; H, 6.35. $C_{15}H_{16}O_4$ requires: C, 69.2; H, 6.2%); ν_{max} 1720, 1615, 1560 and 1515 cm^{-1}; NMR signals at δ 1.73 (3H, bs), 1.76 (3H, bs), 3.92 (3H, s), 4.58 (2H, bd, *J* 7.5 Hz), 5.51 (1H, bt, *J* 7.5 Hz), 6.25 (1H, d, *J* 9.5 Hz), 6.80 (1H, s), 6.88 (1H, s) and 7.59 (1H, d, *J* 9.5 Hz). A mixture of **15** (154 mg), NaOAc (1.1 g) and Ac_2O (15 ml) was refluxed with stirring for 36 hr. Work up as for **4** and chromatography on silica gel 60 with elution with EtOAc–light petroleum (3:17) gave 6 - *acetoxy* - 7 - *methoxy* - 5 - (1,1 - *dimethylallyl*)*coumarin* **18** (151 mg, 80%) colourless plates, m.p. 124–125° (from EtOAc–light petroleum). (Found: C, 67.45; H, 5.85. $C_{17}H_{18}O_5$ requires: C, 67.55; H, 6.0%); ν_{max} 1760, 1728, 1600 and 1560 cm^{-1}; NMR signals at δ 1.55 (6H, s), 2.28 (3H, s), 3.87 (3H, s), 4.97 (1H, dd, *J* 17.5 and 2 Hz), 5.07 (1H, dd, *J* 10 and 2 Hz), 6.15 (1H, d, *J* 9.5 Hz), 6.23 (1H, dd, *J* 17.5 and 10 Hz), 6.80 (1H, s) and 8.23 (1H, d, *J* 9.5 Hz); and **16** (20 mg, 14%) colourless needles, m.p. 166–167° (lit.[26] 167–168°) (from EtOAc–light petroleum) identical (mmp, NMR and TLC) with a sample prepared by acetylation of **14**.

Hydrolysis of **18**

(i) A soln of **18** (56 mg, 0.185 mmole) in MeOH (10 ml) and 2% NaOH/MeOH (3 ml, 1.5 mmole) was stirred for 8 hr until TLC indicated complete disappearance of starting material. Work up as for **7** gave a mixture of two products as an oil. Preparative TLC on sliica (Fluka GF 254) and elution with MeOH–$CHCl_3$–light petroleum (1:4:20) × 3 afforded the *dihydrofuran* **20** (15 mg, 31%) colourless needles, m.p. 154–156° (from EtOAc–light petroleum). (Found: C, 69.0; H, 6.25. $C_{15}H_{16}O_4$ requires: C, 69.2; H, 6.2%); ν_{max} 1725, 1620, 1612 and 1565 cm^{-1}; NMR signals at δ 1.20 (3H, s), 1.42 (3H, d, *J* 6.5 Hz), 1.47 (3H, s), 3.93 (3H, s), 4.46 (1H, q, *J* 6.5 Hz), 6.28 (1H, d, *J* 9.5 Hz), 6.71 (1H, s) and 7.86 (1H, d, *J* 9.5 Hz); and 6 - *hydroxy* - 7 - *methoxy* - 5 - (1,1 - *dimethylallyl*)*coumarin* **17** (31 mg, 65%) tan–yellow plates, m.p. 92–94° (from ether–light petroleum). (Found: C, 69.2; H, 5.95. $C_{15}H_{16}O_4$ requires: C, 69.2; H, 6.2%); ν_{max} 3530, 1720, 1610 and 1570 cm^{-1}; λ_{max} (MeOH) 352, 302, 260 and 238 nm (log ϵ 3.87, 3.81, 3.48 and 3.91); λ_{max} (MeOH + base) 352, 302, 260 and 238 nm (log ϵ 3.85, 3.80, 3.58 and 3.91); NMR signals at δ 1.62 (6H, s), 3.96 (3H, s), 4.95 (1H, dd, *J* 17.5 and 2 Hz), 5.05 (1H, dd, *J* 10 and 2 Hz), 6.00 (1H, s, OH), 6.12 (1H, d, *J* 9.5 Hz), 6.25 (1H, dd, *J* 17.5 and 10 Hz), 6.73 (1H, s) and 8.30 (1H, d, *J* 9.5 Hz).

(ii) A soln of **18** (62 mg, 0.203 mmole) in MeOH (5 ml) and 10% NaOH/MeOH (12 ml, 30 mmole) was stirred for 10 min. Work up as above gave **17** (52 mg, 97%); no trace of **20** could be detected by NMR or TLC.

Methylation of **17**

A mixture of **17** (21 mg), MeI (1.0 ml), K_2CO_3 (100 mg) and acetone (10 ml) was refluxed with stirring for 3 hr. Work up as for **11** gave 6,7 - *dimethoxy* - 5 - (1,1 - *dimethylallyl*)*coumarin* **19** (21 mg) colourless plates, m.p. 75–76° (from light petroleum); mass spectral peaks at *m/z* 274 (M^+, 100%), 259(50), 243(30), 231(27), 128(28) and 115(45); ν_{max} 1720, 1593, 1559 and 1463 cm^{-1}; NMR signals at δ 1.62 (6H, s), 3.75 (3H, s), 3.93 (3H, s), 4.90 (1H, dd, *J* 17.5 and 2 Hz), 5.05 (1H, dd, *J* 10 and 2 Hz), 6.13 (1H, d, *J* 9.5 Hz), 6.25 (1H, dd, *J* 17.5 and 10 Hz), 6.78 (1H, s) and 8.24 (1H, d, *J* 9.5 Hz).

Partial demethylation of 7,8-*dimethoxycoumarin* **22**

A cooled soln of conc H_2SO_4 (27 ml) and water (9 ml) was added to **22** (4.55 g) and the yellow soln stirred in an oil bath kept at 70°.[22] Monitoring by TLC revealed maximal concentration of a new product after 6 days compared with starting material and the more polar 7,8-dihydroxycoumarin. The cooled soln was poured on to crushed ice, extracted with EtOAc, the organic layer washed with brine to neutrality, dried and evaporated. The residue was crystallised from EtOAc–light petroleum to give **21** (3.29 g, 77%), m.p. 173–175° (lit.[22] 173–174°; 29%).

Dimethylpropargylation of **21**

(i) A mixture of **21** (440 mg) in 2% aqueous acetone (30 ml), K_2CO_3 (1.0 g), KI (150 mg) and 3-chloro-3-methylbut-1-yne (1.5 ml) was refluxed with stirring for 12 hr in a closed system. More K_2CO_3 (500 mg), KI (50 mg) and 3-chloro-3-methylbut-1-yne (1.5 ml) were added and refluxing continued for a further 12 hr. Two further additions of 3-chloro-3-methylbut-1-yne (1.5 ml each) were made after 36 and 48 hr. After 60 hr, the mixture was filtered through celite and washed with acetone. The combined filtrates were evaporated and the residue partitioned between EtOAc and water, the organic layer washed with 5% Na_2CO_3 soln, brine, dried and evaporated. The residual oil was chromatographed on silica gel 60. Gradient elution with EtOAc–light petroleum (1:9 to 1:4) afforded 7 - *methoxy* - 8 - (1,1 - *dimethylpropargyloxy*) - 5 - (1,1 - *dimethylpropargyl*)*coumarin* **29** (14 mg, 4%) colourless plates, m.p. 150–152° (from EtOAc–light petroleum). (Found: C, 74.0; H, 6.15. $C_{20}H_{20}O_4$ requires: C, 74.05; H, 6.2%); mass spectral peaks at *m/z* 258 (M^+-C_5H_6, 100%) and 243(79); ν_{max} 3305, 1723, 1590 and 1495 cm^{-1}; NMR signals at δ 1.72 (6H, s), 1.77 (6H, s), 2.30 (1H, s), 2.38 (1H, s), 3.92 (3H, s), 6.25 (1H, d, *J* 9.5 Hz), 6.90 (1H, s) and 8.72 (1H, d, *J* 9.5 Hz); 7 - *methoxy* - 8 - (1,1 - *dimethylpropargyloxy*)*coumarin* **23** (89 mg, 15%) as a pale yellow oil. (Found: C, 69.75; H, 5.85.

$C_{15}H_{14}O_4$ requires: C, 69.75; H, 5.45%); ν_{max} 3300, 1725, 1608 and 1560 cm^{-1}; NMR signals at δ 1.79 (6H, s), 2.30 (1H, s), 3.92 (3H, s), 6.24 (1H, d, *J* 9.5 Hz), 6.86 (1H, d, *J* 8 Hz), 7.21 (1H, d, *J* 8 Hz) and 7.60 (1H, d, *J* 9.5 Hz); and recovered **21** (270 mg).

(ii) A mixture of **21** (208 mg), Cs_2CO_3 (900 mg), 3-chloro-3-methylbut-1-yne (2 ml) and acetone (25 ml) was refluxed with stirring for 36 hr in a closed system. Work up and chromatography as above gave **23** (130 mg, 46%).

Synthesis and Claisen rearrangement of **24**

A soln of **23** (69 mg) in EtOAc (10 ml) was hydrogenated over 5% Pd–$BaSO_4$ (22 mg) for 2.5 hr. Removal of catalyst and solvent followed by flash column chromatography on silica gel (Fluka GF 254) and elution with EtOAc–light petroleum (3:17) gave 7 - *methoxy* - 8 - (1,1 - *dimethylpropoxy*)*coumarin* **25** (13 mg, 17%) colourless needles, m.p. 39–40° (from EtOAc–light petroleum); NMR signals at δ 1.15 (3H, t, *J* Hz), 1.30 (3H, s), 1.85 (2H, q, *J* 7 Hz), 3.88 (3H, s), 6.21 (1H, d, *J* 9.5 Hz), 6.84 (1H, d, *J* 8 Hz), 7.14 (1H, d, *J* 8 Hz) and 7.57 (1H, d, *J* 9.5 Hz); 7 - *methoxy* - 8 - (1,1 - *dimethylallyloxy*)*coumarin* **24** (49 mg, 71%) colourless needles, m.p. 58–59.5° (from EtOAc–light petroleum). (Found: C, 69.15; H, 6.25. $C_{15}H_{16}O_4$ requires: C, 69.2; H, 6.2%); mass spectral peaks at *m/z* 192 (M^+-C_5H_8, 100%), 164(21), 163(29) and 149(36); ν_{max} 1725, 1605, 1560 and 1505 cm^{-1}; NMR signals at δ 1.51 (6H, s), 3.88 (3H, s), 5.00 (1H, dd, *J* 10 and 2 Hz), 5.12 (1H, dd, *J* 17.5 and 2 Hz), 6.20 (1H, d, *J* 9.5 Hz), 6.25 (1H, dd, *J* 17.5 and 10 Hz), 6.83 (1H, d, *J* 8 Hz), 7.15 (1H, d, *J* 8 Hz) and 7.57 (1H, d, *J* 9.5 Hz); and **23** (5 mg, 7%).

A mixture of **24** (27 mg), NaOAc (50 mg) and Ac_2O (1.5 ml) was refluxed with stirring for 90 min. Work up as for **10** gave 7 - *methoxy* - 8 - *acetoxy* - 5 - (1,1 - *dimethylallyl*)*coumarin* **27** (32 mg, 100%) colourless needles, m.p. 159–160° (from EtOAc–light petroleum). (Found: C, 67.55; H, 5.5. $C_{17}H_{18}O_5$ requires: C, 67.55; H, 6.0%); ν_{max} 1760, 1730, 1605 and 1495 cm^{-1}; NMR signals at δ 1.49 (6H, s), 2.38 (3H, s), 3.93 (3H, s), 5.04 (1H, dd, *J* 17.5 and 2 Hz), 5.13 (1H, dd, *J* 10 and 2 Hz), 6.14 (1H, d, *J* 9.5 Hz), 6.15 (1H, dd, *J* 17.5 and 10 Hz), 6.97 (1H, s) and 8.20 (1H, d, *J* 9.5 Hz).

Celerin **26** *and its methyl ether*

A soln of **27** (21 mg, 0.07 mmole) in MeOH (5 ml) and 1% NaOH/MeOH (0.5 ml, 0.125 mmole) was stirred for 15 min. Work up as for **7** gave 7 - *methoxy* - 8 - *hydroxy* - 5 - (1,1 - *dimethylallyl*)*coumarin* (celerin) **26** (18 mg, 100%) colourless plates, m.p. 158–159.5° (lit.[2] 154–156°) (from EtOAc–light petroleum). (Found: C, 69.45; H, 6.15. $C_{15}H_{16}O_4$ requires: C, 69.2; H, 6.2%); mass spectral peaks at *m/z* 260 (M^+, 100%), 245(24), 213(66) and 185(23); ν_{max} 3550, 1730, 1612, 1580 and 1500 cm^{-1}; λ_{max} (MeOH) 325, 264 and 228 nm (log ϵ 4.10, 4.06 and 3.70); λ_{max} (MeOH + base) 332, 284 and 232 nm (log ϵ 3.99, 4.23 and 3.79); NMR signals at δ 1.49 (6H, s), 4.01 (3H, s), 5.01 (1H, dd, *J* 17.5 and 2 Hz), 5.12 (1H, dd, *J* 10 and 2 Hz), 6.14 (1H, dd, *J* 17.5 and 10 Hz), 6.15 (1H, d, *J* 9.5 Hz), 6.93 (1H, s) and 8.22 (1H, d, *J* 9.5 Hz); extremely similar (NMR and mass spectra) to those of a natural sample.

A mixture of **26** (14 mg), K_2CO_3 (150 mg), MeI (0.5 ml) and acetone (10 ml) was refluxed with stirring for 15 min. Work up gave 7,8 - *dimethoxy* - 5 - (1,1 - *dimethylallyl*)*coumarin* **28** (15 mg, 100%) colourless plates, m.p. 99–100° (from light petroleum). (Found: C, 70.2; H, 6.65. $C_{16}H_{18}O_4$ requires: C, 70.05; H, 6.6%); mass spectral peaks at *m/z* 274 (M^+, 100%), 259(64), 231(21), 228(63) and 200(23); ν_{max} 1725, 1590 and 1492 cm^{-1}; NMR signals at δ 1.49 (6H, s), 3.98 (6H, s), 5.02 (1H, dd, *J* 17.5 and 2 Hz), 5.12 (1H, dd, *J* 10 and 2 Hz), 6.14 (1H, dd, *J* 17.5 and 2 Hz), 6.14 (1H, d, *J* 9.5 Hz), 6.93 (1H, s) and 8.18 (1H, d, *J* 9.5 Hz).

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