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# An Improved Synthesis of 3-(1,1-Dimethylallyl)coumarins

**Rosario Hernández-Galán, Javier Salvá, Guillermo M. Massanet and Isidro G. Collado***

Departamento de Química Orgánica. Facultad de Ciencias, Universidad de Cádiz. Apdo. 40, 11510 Puerto Real, Cádiz, SPAIN.

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***Abstract:*** The syntheses of several 3-(1,1-dimethylallyl)coumarins, simple or bearing additional furan or pyran rings is achieved starting from the corresponding C-3 unsubstituted derivatives. The key step involves Ireland-Claisen rearrangements of allyl esters.

## INTRODUCTION

3-Isoprenyl coumarins possess a wide range of biological properties.[1] It has been widely reported their spasmolytic,[2] cytostatic,[3] molluscicidal,[4] antifertility[5] or frijol seed germination inhibition[6] activities. Studies on the relationship between cytostatic activity and structure suggest that the nature of the side chain and its location on the coumarinic skeleton are important requirements for the activity.[3] These facts together with the small amounts in which they are obtained from natural sources, mainly Rutaceae plants, have focused research directed towards their synthesis in good overall yields.

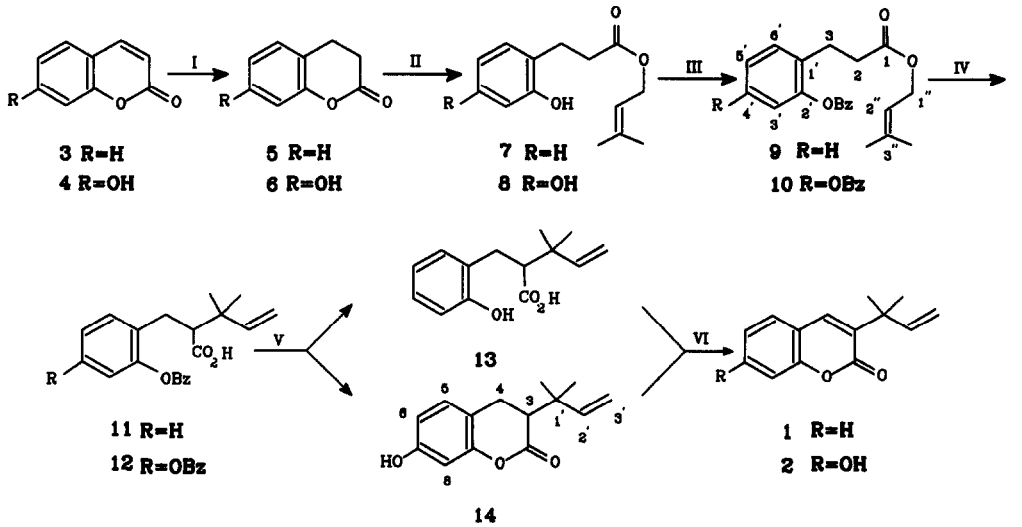
Two strategies had been developed to obtain 3-isoprenylcoumarins. Both approaches involve sigmatropic rearrangements of allylethers: one of 7 or 5-oxygenated coumarins,[7] the other of 4-hydroxy derivatives and subsequent elimination.[8]

On a recent communication[9] we reported a new route towards the syntheses of 3-(1,1-dimethylallyl)-coumarins through a different strategy which involves an Ireland-Claisen rearrangement[10] and leads to an important improvement in yields. In the present paper the preparation through this method of several 3-(1,1-dimethylallyl) coumarins with additional furan or pyran rings is described.

## RESULTS AND DISCUSSION

The syntheses of 3-(1,1-dimethylallyl)coumarin (**1**) and angustifolin (**2**) following the strategy above mentioned (scheme 1) involves catalytic hydrogenation of coumarin (**3**) and umbelliferone (**4**) respectively and treatment of the corresponding dihydroderivatives **5** and **6** with sodium 3-methyl-2-butenoxide to afford the esters **7** and **8**. Benzylation of **7** and **8** gave the benzyl ethers **9** and **10** and the $\gamma,\partial$-unsaturated acids **11** and **12** were obtained by Ireland-Claisen rearrangement via the *O*-trimethylsilyl ethers of the ester enolates. Treatment of **11** and **12** with $BBr_3$ lead to the phenol **13** and dihydrocoumarin **14**. The desired 3-(1,1-

dimethylallyl)coumarin derivatives were obtained refluxing **13** and **14** in diphenyl ether with Pd-charcoal[9] to afford 3-(1,1-dimethylallyl)coumarin (**1**) and angustifolin (**2**). Angustifolin (**2**) is a key precursor for the preparation of many 3-(1,1-dimethylallyl)coumarins.[11] The synthesis above described leads to a 47% overall yield.



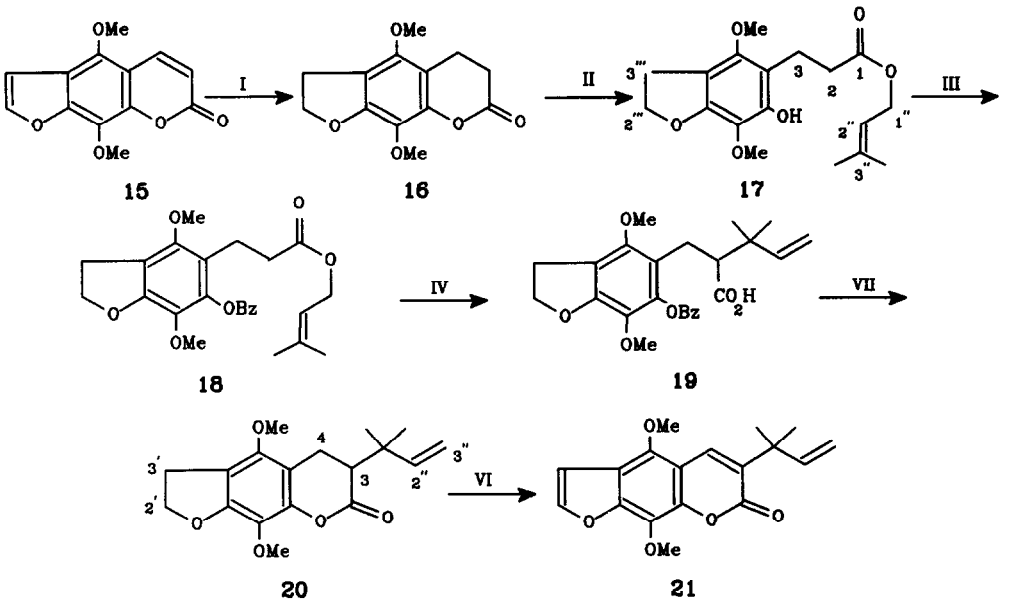

I) $H_2$, Pd-charcoal/AcOH; II) 3-methyl-2-buten-1-ol,Na/acetone; III) BzBr,$K_2CO_3$/acetone; IV) LDA/THF,$Me_3SiCl$; V) $BBr_3$, $CH_2Cl_2$/-22°C→r.t.; VI) $Ph_2O$,reflux,Pd-charcoal

**Scheme 1**

Furanocoumarins are an important group of bioactive natural products showing antimutagenic[12] and photosensitizing properties on human skin and on several other biological systems,[13] together with their ability to react photochemically with the DNA macromolecule.[14] The alkylation at C-3 on furanocoumarins has been carried out following the pathway outlined in scheme 2. Catalytic hydrogenation of isopimpinellin[15] (**15**) on Pd-charcoal/AcOH afforded the tetrahydro derivative **16** in quantitative yield. Treatment of **16** with sodium 3-methyl-2-butenoxide leads to the ester **17** (80%) through ∂-lactone ring opening.

The ester **17** bear the allylic alcohol moiety required to afford a γ,∂-unsaturated carboxylic acid through Ireland-Claisen rearrangement. Nevertheless, as we previously reported for **7** and **8**,[9] attempts to achieve the reaction directly on the phenol were unsuccessful. Thus the hydroxyl group was previously protected by treatment of the ester **17** with benzyl bromide and $K_2CO_3$/acetone leading to the corresponding benzyloxy derivative **18** (83%). The rearrangement of **18** afforded the acid **19** (90%).

To avoid cleavage of the methoxyl groups, deprotection and ring closure in **19** was carried out under milder conditions than those reported for **11** and **12**. Thus treatment of **19** with $BCl_3$ in $CH_2Cl_2$ at -22° C for 3 h and subsequently 1h at room temperature leads to the tetrahydroderivative properly functionalized at C-3 **20** (66%).



VII) $BCl_3$,$CH_2Cl_2$/-22°C→r.t.

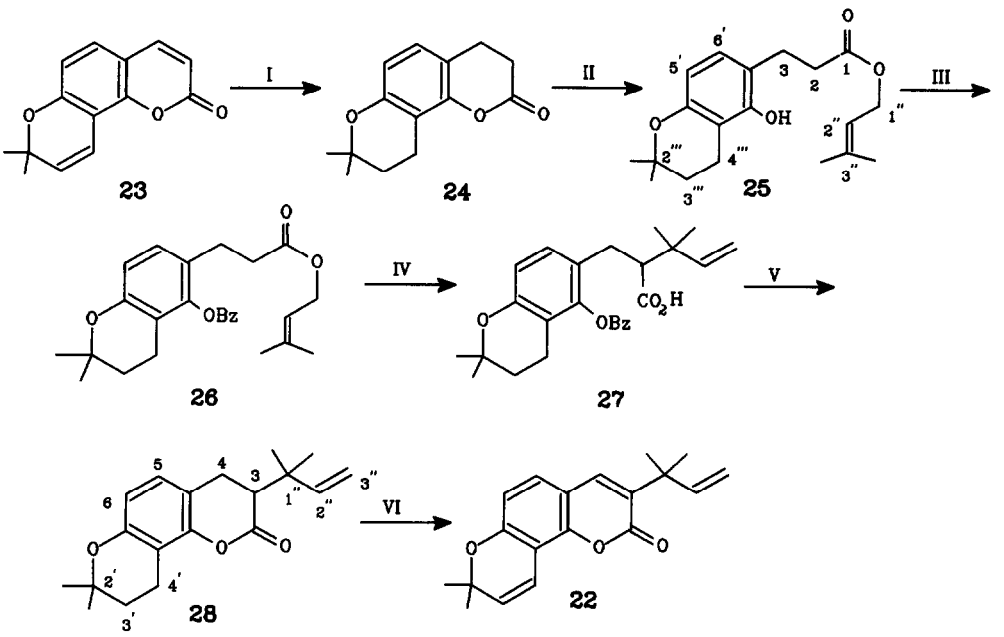
**Scheme 2**

The desired 3-(1,1-dimethylallyl)furocoumarin, dimethoxychalepensin (**21**) is a natural compound isolated from the callus culture of *Ruta graveolens*.[16] **21** was obtained refluxing tetrahydroderivative **20** in diphenyl ether with Pd-charcoal (63%). No authentic sample of **21** was available but the structure of the synthetic compound was unequivocally assigned by analysis of spectral

data. Thus the mass spectrum showed the molecular ion at $m/z$ = 314 in agreement with the molecular formula $C_{18}H_{18}O_5$. In the $^1H$ NMR spectrum several isolated spin systems were observed. The signals at $\partial$ 5.58 (dd,1H,J=17.6 and 10.6 Hz), 5.02 (d,1H,J=17.6 Hz), 5.00 (d,1H,J=10.6 Hz) and 1.61 (s,6H) are typical of the 1,1-dimethylallyl moiety. The AB system at $\partial$ 7.56 (d,1H,J=2.2 Hz) and 7.05 (d,1H,J=2.2 Hz) was assigned to the furanic protons. Two singlets at 4.10 (s,3H) and 3.99 (s,3H) ascertained the presence of two methoxyl groups. The remaining signal at $\partial$ 7.79 (s,1H) is typical of 3-alkyl coumarins. These data are completely compatible with the proposed structure.

In order to test the synthetic strategy to obtain 3-(1,1-dimethylallyl)pyranocoumarins the synthesis of 3-(1,1-dimethylallyl)seselin (**22**) from seselin (**23**) was attempted.

Catalytic hydrogenation lead to tetrahydroderivative (**24**) (97%) and treatment with sodium 3-methyl-2-butenoxide afforded the ester **25** (72%) (Scheme 3). Ireland-Claisen rearrangement of the benzyloxy derivative **26** (96%) gave $\gamma,\partial$-unsaturated acid **27** (85%). Tetrahydroderivative **28** was prepared by treatment of **27** with $BBr_3$ in $CH_2Cl_2$ (63%). To obtain 3-(1,1-dimethylallyl)seselin (**29**), **35** was refluxed in diphenyl ether with Pd-charcoal affording the 3-(1,1-dimethylallyl) derivative **22** in 50% yield.




**Scheme 3**

It is worth noting that no C-3 unsubstituted derivative was detected when the respective ∂-lactone derivatives **20** and **28** were heated in diphenyl ether with Pd-charcoal. This fact is in agreement with the explanation proposed[9] for the formation of coumarin (**3**) from the corresponding coumarinic acid derivative (**13**) through a Pd-catalyzed [3,3]-sigmatropic rearrangement.

In conclusion, the method described for the synthesis of angustifolin (**2**) from umbelliferone (**4**) is extended to the syntheses of dimethoxychalepensin (**21**) and 3-(1,1-dimethylallyl)seselin (**22**) from the corresponding C-3 unsubstituted derivatives with 25% and 18% overall yields, respectively, showing that the strategy herein described can be used as a general method to obtain 3-(1,1-dimethylallyl) coumarins.

## EXPERIMENTAL

Melting points were determinated in a Kofler block Reichert-Jung apparatus and are uncorrected. Infrared spectra were recorded in a Perkin-Elmer 881 spectrophotometer. UV were registered on a Phillips P 3250. $^1$H-NMR were made on a Varian Gemini 200 and Varian XL-200 using $SiMe_4$ as internal reference. Mass spectra were recorded on a V G 12-250 spectrometer using 70 eV.Thin layer chromatography was done on MN Alugram SIL G/UV 254 plates, o.25 mm thick. Merck silica gel was used for column chromatography.

**General procedure for the catalytic hydrogenation : hydrogenation of umbelliferone (4).**

6.20 mmol of **4** were dissolved in 100 ml of acetic acid. 100 mg of Pd-charcoal were added and the mixture was subjected to hydrogenation under 1.25 atm. pressure of $H_2$. When starting material disappeared, as ascertained by tlc, the reaction was stopped (24 h.). The catalyst was filtered through celite and evaporation

of the solvent by distillation under reduced pressure furnished 6,20 mmol (quantitative yield) of 3,4-dihydroumbelliferone (**6**): **mp** 125-126ºC (EtOAc);**IR** (KBr) 3355,1731,1621,1505,1142 $cm^{-1}$; **UV** (MeOH) $\lambda_{max}$ 291, 249 nm; **$^1$H-NMR** ($CDCl_3$) $\partial$ 7.08 (d, 1H, J=8.2 Hz, H-5), 6.60 (dd, 1H, J=8.2 and J=2.5 Hz, H-6), 6.49 (d, 1H, J=2.5 Hz, H-8), 2.97-2.71 (m, 4H, H-3 and H-4); **EIMS** m/z 164 (100), 136 (45), 122 (27), 107 (19), 94 (23).

**Catalytic hydrogenation of isopimpinellin (15):** 5.60 mmol of **15** and 400 mg of Pd-charcoal in 100 ml of acetic acid were subjected to hydrogenation as described above yielding 5.60 mmol of 3,4,2',3'-tetrahydroisopimpinellin (**16**) (quantitative yield): **mp** 97-98ºC; **IR** (film) 1768, 1604, 1474, 1423, 1246, 1087, 1050 $cm^{-1}$; **UV** (MeOH) $\lambda_{max}$ 209 nm; **$^1$H-NMR** ($CDCl_3$) $\partial$ 4.60 (t, 2H, J=8.6 Hz, H-2'), 3.86 (s, 3H, -OMe), 3.78 (s, 3H, -OMe), 3.26 (t, 2H, J=8.6 Hz, H-3'), 2.91-2.62 (m, 4H, H-3 and H-4); **EIMS** m/z 250 (100), 235 (32), 208 (51), 193 (46), 180 (37), 165 (43).

**Catalytic hydrogenation of seselin (23):** 3.00 mmol of **23** and 200 mg of Pd-charcoal in 75 ml of acetic acid were subjected to hydrogenation as described above yielding 2.90 mmol of 3,4,3'4'-tetrahydroseselin (**24**) (97%): **mp** 98-99ºC; **IR** (KBr) 2973, 2918, 1754, 1435, 1128, 1072, 819 $cm^{-1}$; **UV** (MeOH) $\lambda_{max}$ 281,208 nm; **$^1$H-NMR** ($CDCl_3$) $\partial$ 6.89 (d,1H, J=8.4 Hz, H-5), 6.54 (d,1H, J=8.4 Hz, H-6), 2.93-1.70 (m, 6H, H-3, H-4, and H-3'), 1.77 (t, 2H, J=6.8 Hz, H-4'), 1.31 (s, 6H, C-2'-$Me_2$); **EIMS** m/z 232 (64), 189 (73), 177 (100), 148 (33), 135 (51), 91 (24).

**General procedure for $\partial$-lactone ring opening: 3,3-dimethylallyl ester of 2,3-dihydro-*o*-coumaric acid (7).**

1.60 mmol of 3,4-dihydrocoumarin (**5**) were dissolved in 5 ml of acetone and 0.15 ml of sodium 3-methyl-2-butenoxide (prepared by addition of sodium to an excess of 3-methyl-2-buten-1-ol) were added. The mixture was stirred at room temperature for 2 h, neutralized with 2 N HCl and extracted with EtOAc. The organic layer was washed with brine and dried over anhydrous $Na_2SO_4$. Evaporation of the solvent afforded an oily residue which was purified by CC (hexane:EtOAc) yielding **7** (1.36 mmol, 85%): oil; **IR** (film) 3400, 1700, 1591, 1490, 1228, 1096, 751 $cm^{-1}$; **UV** (MeOH) $\lambda_{max}$ 275, 219 nm; **$^1$H-NMR** ($CDCl_3$) $\partial$ 7.10-6.76 (m, 4H, aromatic protons), 5.24 (br t, 1H, J=7.3 Hz, H-2"), 4.53 (d, 2H, J=7.3 Hz, H-1"), 2.87-2.62 (m, 4H, H-2 and H-3), 1.69 (s, 3H, C-3"-Me); 1.63 (s, 3H, C-3"-Me); **EIMS** m/z 234 (1), 166 (83), 148 (100), 120 (62), 69 (99).

**3,3-dimethylallyl ester of 2,3-dihydro-p-hydroxy-*o*-coumaric acid (8): 8** (0.82 mmol) was obtained from **6** (0.93 mmol) as described above in the general procedure (88%): oil; **IR** (film) 3362,1700,1602,1508, 1159, 836 $cm^{-1}$; **UV** (MeOH) $\lambda_{max}$ 281, 225 nm;**$^1$H-NMR** ($CDCl_3$) $\partial$ 6.84 (d,1H, J=8.0 Hz, H-6'), 6.33 (d,1H, J=2.5 Hz, H-3'), 6.29 (dd, 1H, J=8.0 Hz and J=2.5 Hz, H-5'), 5.23 (br t, 1H, J=7.5 Hz, H-2"), 4.52 (d, 2H, J=7.5 Hz, H-1"), 2.78-2.58 (m, 4H, H-2 and H-3), 1.68 (s, 3H, C-3"-Me), 1.62 (s, 3H, C-3"-Me), **EIMS** m/z 250 (4), 182 (43), 164 (78), 136 (34), 123 (45), 64 (100).

**3,3-dimethylallyl ester of dihydrocoumaric acid derivative 17:** Compound **17** (1.2 mmol) was obtained from

**16** (1.5 mmol) as described above in the general procedure (80%): oil; **IR** (film) 3422, 2943, 1712, 1606, 1377, 1264, 1158, 1078 $cm^{-1}$; **UV** (MeOH) $\lambda_{max}$ 208 nm; **$^1$H-NMR** ($CDCl_3$) $\partial$ 6.14 (s, 1H, -OH), 5.70 (br t, 1H, J=7.0 Hz, H-2"), 4.57 (t, 2H, J=8.5 Hz, H-2'"), 4.55 (d, 2H, J=7.0 Hz, H-1"), 3.88 (s, 3H, -OMe), 3.77 (s, 3H, -OMe), 3.22 (t, 2H, J=8.5 Hz, H-3'"), 2.88-2.58 (m, 4H, H-2 and H-3), 1.74 (s, 3H, C-3"-Me), 1.69 (s, 3H, C-3"-Me); **EIMS** m/z 336 (60), 268 (73), 250(37), 209 (100), 69 (37).

**3,3-Dimethylallyl ester of dihydrocoumaric acid derivative 25:** Compound **25** (0.86 mmol) was obtained from **24** (1.20 mmol) as described above in the general procedure (72%): oil; **IR** (film) 3349, 2926, 2855, 1716, 1590, 1447, 1380, 1160,1048 $cm^{-1}$; **UV** (MeOH) $\lambda_{max}$ 209 nm; **$^1$H-NMR** ($CDCl_3$) 7.59 (br t, 1H, -OH), 6.79 (d, 1H, J=8.5 Hz, H-6'), 6.34 (d, 1H, J=8.5 Hz, H-5'), 5.32 (br t, J=7.3 Hz, H-2"), 4.57 (d, 2H, J=7.3 Hz), H-1"), 2.65-2.82 (m, 6H, H-2, H-3 and H-4'"), 1.73 (s, 3H, C-3"-Me), 1.68 (s, 3H, C-3"- Me), 1.65 (t, 2H, J=6.8 Hz, H-3'"), 1.29 (s, 3H, C-2"'-Me), 1.24 (s, 3H, C-2"'-Me); **EIMS** m/z 318 (8), 250 (52), 232 (30), 191 (94), 177 (100), 135 (91).

**General procedure of benzylation: 3,3-dimethylallyl ester of *O*-benzyl-2,3-dihydro-*o*-coumaric acid (9).**

To a refluxing mixture of 2.10 mmol of **7** and 650 mg of $K_2CO_3$ in 40 ml of acetone, 0.5 ml of benzyl bromide were added. The reaction mixture was refluxed for 48 hours, then filtered and the solvent removed. The oily residue was dissolved in EtOAc, washed with saturated solution of $NaHCO_3$ and brine and dried over anhydrous $Na_2SO_4$. Evaporation of the solvent afforded a reaction crude which was purified by CC (hexane:EtOAc, 9:1) yielding **9** (1.93 mmol, 92%): oil; **IR** (film) 1727, 1589, 1490, 1238, 1022, 749 $cm^{-1}$; **UV** (MeOH) $\lambda_{max}$ 272, 206 nm; **$^1$H-NMR** ($CDCl_3$) $\partial$ 7.48-6.83 (m, 9H, aromatic protons), 5.29 (br t, 1H, J=7.3 Hz, H-2"), 5.08 (s, 2H, -O-$CH_2$-$\phi$), 4.54 (d, 2H, J=7.3 Hz, H-1"), 2.96-2.60 (m, 4H, H-2 and H-3), 1.74 (s, 3H, C-3"-Me), 1.67 (s, 3H, C-3'-Me); **EIMS** m/z 324 (1); 256 (9); 165 (4); 148 (14); 129 (4); 105 (5); 91 (100); 69 (14).

**3,3-dimethylallyl ester of *p*-benzyloxy-*O*-benzyl-2,3-dihydrocoumaric acid (10):** 1.10 mmol of **8** was subjected to the treatment described above for **7** yielding 0.93 mmol **10** (83%):oil; **IR** (film) 1724, 1606, 1497, 1255, 1024, 1164, 828, 732, 694 $cm^{-1}$; **UV** $\lambda_{max}$ 289, 223, 215, 207 nm; **$^1$H-NMR** ($CDCl_3$): 7.38-7.25 (m, 10H, O-Bz aromatic protons), 7.01 (d, 1H, J=8.2 Hz , H-6'), 6.52 (d, 1H, J=2.5 Hz, H-3'), 6.44 (dd, 1H, J=8.2 Hz and J=2.5 Hz, H-5'), 5.25 (br t, 1H, J=7.2 Hz, H-2"), 4.99 (s, 2H, O-$CH_2$-$\phi$), 4.95 (s, 2H, O-$CH_2$-$\phi$), 4.50 (d, 2H, J=7.2 Hz, H-1"), 2.93-2.52 (m, 4H, H-2 and H-3), 1.70 (s, 3H, C-3"-Me), 1.63 (s, 3H, C-3'-Me); **EIMS** m/z 430 (23); 361 (21); 181 (64); 91 (100); 69 (46); 41 (41).

**3,3-dimethylallyl ester of dihydrocoumaric acid derivative 18**: 1.37 mmol of **17** and 207 mg of $K_2CO_3$ in 15 ml of acetone were refluxed and 0.4 ml of benzyl bromide were added. The reaction mixture was refluxed for 5 days and the resulting crude material was extracted as indicated for **9** and purified by CC (hexane:EtOAc, 9:1) yielding 1.14 mmol (83%) of **18**: oil; **IR** (film) 2937, 1723, 1595, 1424, 1353, 1267, 1159, 1084, 1050 $cm^{-1}$; **UV** (MeOH) $\lambda_{max}$ 209 nm; **$^1$H-NMR** ($CDCl_3$) $\partial$ 7.50-7.34 (m, 5H, O-Bz aromatic protons), 5.33 (br t,

1H, J=7.1 Hz, H-2"), 5.02 (s, 2H, -O-$CH_2$-ϕ), 4.61 (t, 2H, J=8.6 Hz, H-2"'), 3.88 (s, 3H, -OMe), 3.78 (s, 3H, -OMe), 3.29 (t, 2H, J=8.6 Hz, H-3"'), 2.89-2.38(m, 4H, H-2 and H-3), 1.76 (s, 3H, C-3"-Me), 1.69 (s, 3H, C-3"-Me); **EIMS** m/z 426 (7), 258 (11), 266 (15), 250 (11), 239 (11), 209 (24), 193 (20), 91 (100), 77 (15), 69(55), 65 (18).

**3,3-dimethylallyl ester of dihydrocoumaric acid derivative 26:** To a refluxing mixture of 0.75 mmol of starting material (**25**) and 350 mg of $K_2CO_3$ in acetone, 0.25 ml of benzyl bromide were added. The reaction mixture was refluxed for 24 h and extracted as indicated for **9** yielding 0.72 mmol of **26** (96%): oil; **IR** (film) 2980, 2937, 1723, 1601, 1476, 1366, 1271, 1157, 1118, 1065, 1015, 980, 915, 810, 734, 696 $cm^{-1}$; **UV** (MeOH) $\lambda_{max}$ 218, 209 nm; **$^1$H-NMR** ($CDCl_3$) ∂ 7.50-7.37 (m, 5H, O-Bz aromatic protons), 6.93 (d, 1H, J=8.5 Hz, H-6'), 6.54 (d, 1H, J=8.5 Hz, H-5'), 5.32 (br t, 1H, J=7.3 Hz, H-2"), 4.86 (s, 2H, -O-$CH_2$-ϕ), 4.56 (d, 2H, J=7.3 Hz, H-1"), 2.89-2.63 (m, 6H, H-2, H-3 and H-4"'), 1.75 (t, 2H, J=6.7 Hz, H-3"'), 1.75 (s, 3H, C-3"-Me), 1.69 (s, 3H, C-3"-Me), 1.35 (s, 6H, C-2"'-$Me_2$); **EIMS** m/z 408 (9), 340 (28), 249 (22), 91 (100), 83 (45), 69 (64).

**General Procedure for the Ireland-Claisen rearrangement: 2-(1,1-dimethylallyl)-2,3-dihydro-*O*-benzylcoumaric acid (11).**

To a solution of 0.80 mmol of LDA in 10 ml of THF at -95ºC (acetone/$N_2$) 0.47 mmol of ester **9** in 5 ml of THF were added. The reaction mixture was stirred at -95ºC for 1h, and 0.50 mmol of trimethylchlorosilane were added. After stirring for 1h at -95ºC the mixture was allowed to warm up to 25ºC and stirred for 18 h. The solution was poured into 75 ml of 5% aqueous NaOH and stirred for 10 min at 25 ºC. The aqueous layer was washed with ether, the aqueous phase was acidified with concentrated HCl and extracted repeatedly with $CH_2Cl_2$. The combined extracts were dried over $Na_2SO_4$ and concentrated under reduced pressure. The crude extract thus obtained was purified by CC (hexane:EtOAc, 7:3) to obtain the desired **11** (0.46 mmol, 98%): **mp** 124-125ºC (hexane: EtOAc); **IR** (KBr) 1700, 1596, 1489, 1236, 1108, 748, 695 $cm^{-1}$; **UV** (MeOH) $\lambda_{max}$ 272, 205 nm; **$^1$H-NMR** ($CDCl_3$) ∂ 7.49-7.44 (m, 9H, aromatic protons), 5.75 (dd, 1H, J=17.4 Hz and J=10.7 Hz, H-2"), 5.02(s, 2H, -O-$CH_2$-ϕ), 4.94 (dd, 1H, J=17.4 Hz and J=1.3 Hz, trans H-3"), 4.88 (dd, 1H, J=10.7 Hz and J=1.3 Hz, cis H-3"), 2.96-2.65 (m, 3H, H-2 and H-3), 1.06 (s, 3H, C-1"-Me), 1.02 (s, 3H, C-1"-Me), **EIMS** m/z 324 (4), 216 (6), 165 (7), 148 (15), 107 (8), 91 (100), 69 (10).

**2-(1,1-dimethyallyl)-2,3-dihydro-*O*-benzyl-*p*-benzyloxycoumaric acid (12): 12** was prepared from **10** according to the procedure above described for the obtention of **11**. 0.36 mmol of ester **10** afforded 0.33 mmol of **12** (92%): **mp** 87-88ºC (hexane:EtOAc); **IR** (KBr) 1701, 1603, 1498, 1252, 1025, 831, 733, 694 $cm^{-1}$; **UV** (MeOH) $\lambda_{max}$ 322, 218, 207 nm; **$^1$H-NMR** ($CDCl_3$) 7.34-7-20 (m, 10H, O-Bz aromatic protons), 6.93 (d, 1H, J=8.0 Hz, H-6'), 6.51 (d, 1H, J=2.3 Hz, H-3'), 6.37 (dd, 1H, J=8.0 Hz and J=2.3 Hz, H-5'), 5.7 (dd, 1H, J=17.4 and 10.7 Hz, H-2"), 4.92 (s, 4H, -O-$CH_2$-ϕ), 4.90 (d, 1H, J=17.4, trans H-3"), 4.84 (d, 1H, J=10.7 Hz, cis H-3"), 2.96-2.59(m, 3H, H-2 and H-3), 1.02 (s, 3H, C-1"-Me), 0.98 (s, 3H, C-1"-Me); **EIMS** m/z 430 (1), 303 (1), 181 (7), 123 (1), 91 (100).

**2-(1,1-dimethylallyl) dihydrocoumaric acid derivative 19:** Compound **19** was prepared from **18** according to the procedure above described. 1.14 mmol of ester **18** afforded 1.03 mmol of **19** (90%): **mp** 91-93ºC; **IR** (KBr) 3484, 3037, 2966, 1696, 1591, 1467, 1423, 1346, 1242, 1083, 1051, 986 $cm^{-1}$; **UV** (MeOH) 288 nm; **$^1$H-NMR** ($CDCl_3$) $\partial$ 7.44-7.32 (m, 5H, O-Bz aromatic protons), 5.87 (dd, 1H, J=17.5 Hz and J=10.7 Hz, H-2"), 4.99 (m, 4H, -O-$CH_2$-$\phi$, cis and trans H-3"), 4.58 (t, 2H, J=8.6 Hz, H-2'''), 3.83 (s, 3H, -OMe), 3.71 (s, 3H, -OMe), 3.26 (t, 2H, J=8.6 Hz, H-3'''), 2.94-2.47 (m, 3H, H-2 and H-3), 1.07 (s, 3H, C-1"-Me), 1.04 (s, 3H, C-1"-Me); **EIMS** m/z 426 (14), 299 (16), 275 (14), 249 (15), 209 (59), 91 (100), 69 (35).

**2-(1,1-dimethylallyl)dihydrocoumaric acid derivative 27: 27** was prepared from **26** according to the general procedure. 0.52 mmol of **26** afforded 0.44 mmol of **27** (85%): oil; **IR** (KBr) 3500-2500, 2979, 1697, 1578, 1476, 1364, 1235, 1158, 1117, 1058, 913, 807, 743, 695 $cm^{-1}$; **UV** (MeOH) 208 nm; **$^1$H-NMR** ($CDCl_3$) $\partial$ 7.48-7.36 (m, 5H, O-Bz aromatic protons), 6.89 (d, 1H, J=8.5 Hz, H-6') 6.50 (d, 1H, J=8.5 Hz, H-5'), 5.81 (dd, 1H, J=17.5 Hz and J=10.7 Hz, H-2"), 4.97 (d, 1H, J=17.5 Hz, trans H-3"), 4.92 (d, 1H, J=10.7 Hz, cis H-3"), 4.82 (s, 2H, -O-$CH_2$-$\phi$), 2.83-2.63 (m, 5H, H-2, H-3, and H-4'''), 1.73 (t, 2H, J=6.6 Hz, H-3'''), 1.32 (s, 3H, C-2'''-Me), 1.29 (s, 3H, C-2'''-Me), 1.09 (s, 3H, C-1"-Me), 1.05 (s, 3H, C-1"-Me); **EIMS** m/z 408 (53), 281 (26), 191(77), 91 (100), 69(26).

**General treatment with $BBr_3$:2-(1,1-dimethylallyl)-2,3-dihydro-*o*-coumaric acid (13).**

0.05 ml of $BBr_3$ were added to 0.38 mmol of **11** dissolved in 10 ml of dry $CH_2Cl_2$ at -22 ºC ($CCl_4/N_2$). The reaction mixture was stirred at -22ºC for 1 h. Then was allowed to warm up to room temperature and stirred until the starting material had disappeared (2h) as ascertained by tlc. The reaction mixture was poured in ice water and extracted with EtOAc. The organic phase was washed with a saturated solution of $NaHCO_3$ and brine, dried over anhydrous $Na_2SO_4$ and the solvent was removed by distillation under reduced pressure. The crude material obtained was purified by CC (hexane:EtOAc, 7:3) yielding **13** (0.33 mmol, 87%): **mp** 99-100ºC (hexane:EtOAc); **IR** (film) 3400, 1700, 1233, 750 $cm^{-1}$; **UV** (MeOH) $\lambda_{max}$ 278, 220, 203 nm; **$^1$H-NMR** ($CDCl_3$) $\partial$ 7.08-7.01 (m, 2H, H-4' and H-6'), 6.86-6.76 (m, 2H, H-3' and H-5'), 5.94 (dd, 1H, J=17.9 Hz and J=10.4 Hz, H-2"), 5.10 (dd, 1H, J=10.3 Hz and J=1.1 Hz, cis H-3"), 5.08 (dd, 1H, J=17.9 Hz and J=1.1 Hz, trans H-3"), 2.88-2.60 (m, 3H, H-2 and H-3), 1.18 (s, 6H, C-1"-$Me_2$); **EIMS** m/z 234 (10); 216 (24); 173 (20); 148 (89); 120 (22); 107 (68); 69 (100).

**3-(1,1-dimethylallyl)-3,4-dihydroumbelliferone (14): 14** was prepared according to the procedure described above for the obtention of **13**. Thus 0.15 mmol of **12** afforded 0.14 mmol of **14** (93%): oil; **IR** (film) 3400, 1723, 1610, 1506, 1455, 1109, 845 $cm^{-1}$; **UV** (MeOH) $\lambda_{max}$ 281, 204 nm; **$^1$H-NMR** ($CDCl_3$) $\partial$ 7.40 (br s, O-H), 6.57 (d, 1H, J=8.6 Hz, H-5), 6.53 (dd, 1H, J=8.6 and 2.2 Hz, H-6), 6.51 (d, 1H, J=2.2 Hz, H-8), 5.86 (dd, 1H, J=17.8 Hz and J=10.3 Hz, H-2'), 5.02 (d, 1H, J=10.3 Hz, cis H-3'), 5.00 (d, 1H, J=17.8 Hz, trans H-3'), 2.93-2.83 (m, 3H, H-3 and H-4), 1.14 (s, 3H, C-1'-Me), 1.25 (s, 3H, C-1'-Me); **EIMS** m/z 232 (15); 189 (20); 163 (83); 134 (25); 123 (55); 107 (20); 83 (22); 77 (24); 69 (100); 53 (25); 41 (92).

**3-(1,1-dimethylallyl)-3,4,2',3'-tetrahydroisopimpinellin (20): 20** was prepared through a similar procedure

to that described for **13**, but $BCl_3$ was used instead of $BBr_3$. 0.03 mmol of **19** afforded 0.02 mmol of **20** (66%): oil; **IR** (film) 2929, 1759, 1604, 1251, 1212, 110, 1055, 920, 750, 665 $cm^{-1}$; **UV** (MeOH) $\lambda_{max}$ 208 nm; **$^1$H-NMR** (400 MHz) ($CDCl_3$) $\partial$ 5.85 (dd, 1H, J=17.6 Hz and 10.6 Hz, H-2"), 4.99 (dd, 1H, J=10.6 and J=1.1 Hz, cis H-3"), 4.99 (dd, 1H, J=17.6 Hz and J=1.1 Hz, trans H-3"), 4.61 (br t, 2H, J=8.6 Hz, H-2'), 3.86 (s, 3H, -OMe), 3.77 (s, 3H, -OMe), 3.26 (br t, J=8.6 Hz, H-3'), 2.97 (dd, 1H, J=16.5 Hz and J=6.4 Hz, H-4), 2.75 (dd, 1H, J=16.5 Hz and J=9.2 Hz, H-4), 2.48 (dd, J=9.2 Hz and J=6.4 Hz, H-3), 1.19 (s, 3H, C-1"-Me), 1.16 (s, 3H, C-1"-Me). **EIMS** m/z 318 (83), 248 (51), 208 (51), 193 (31), 179 (298), 165 (25), 149 (24), 91 (28), 77 (45), 69 (71), 57 (65), 41 (100).

**3-(1,1-dimethylallyl)-3,4,3',4'-tetrahydroseselin (28):** Compound **28** was prepared according to the procedure described above for **13**. Thus 0.16 mmol of **27** afforded 0.10 mmol of **28** (63%): oil; **IR** (film) 2939, 2874, 1752, 1432, 1380, 1258, 1148, 1102, 1015, 917, 806 $cm^{-1}$; **UV** (MeOH) $\lambda_{max}$ 209 nm; **$^1$H-NMR** ($CDCl_3$) $\partial$ 6.83 (d, 1H, J=8.3 Hz, H-5), 6.50 (d, 1H, J=8.3 Hz, H-6), 5.85 (dd, 1H, J=17.6 Hz and J=10.5 Hz, H-2"), 4.99 (d, 1H, J=17.6 Hz, trans H-3"), 4.98 (d, 1H, J=10.5 Hz, cis H-3"), 2.87-2.67 (m, 4H, H-4 and H-3'), 2.53 (dd, 1H, J=9.5 Hz and J=6.7 Hz, H-3), 1.76 (br t, 2H, J=6.7 Hz, H-4'), 1.29 (s, 6H, C-2'-$Me_2$), 1.21 (s, 3H, C-1"-Me), 1.16 (s, 3H, C-1"-Me); **EIMS** m/z 300 (100), 230 (44), 175 (28), 69 (32).

**General Treatment with Pd-Charcoal: 3-(1,1-dimethylallyl)coumarin (1).**

0.11 mmol of **13** were dissolved in 10 ml of diphenyl ether and 25 mg of Pd-charcoal were added. The mixture was refluxed for 3 h, then it was cooled, filtered over celite and purified by CC yielding 3-(1,1-dimethylallyl)coumarin (**1**) (0.03 mmol, 27 %) and coumarin (**3**) (0.08 mmol, 73%). 3-(1,1-Dimethyl allyl)coumarin (**1**): oil (Lit [17] 67-68 ºC); **IR** (film) 1732, 1575, 145, 1230, 1108 $cm^{-1}$; **UV** (MeOH) $\lambda_{max}$ 260, 224 nm; **$^1$H-NMR** ($CDCl_3$) $\partial$ 7.52 (s, 1H, H-4), 7.25 (m, 4H, aromatic protons), 6.13 (dd, 1H, J=17.0 Hz and J=10.0 Hz, H-2'), 4.93 (d, 1H, J=10.0 Hz, cis H-3'), 4.88 (d, 1H, J=17.0 Hz, trans H-3'), 1.53 (s, 6H, C-1'-$Me_2$); **EIMS** m/z 214 (69), 199 (49), 149 (100).

**Angustifolin (2):** Compound **2** was prepared from **14** according to the procedure above described for the obtention of **1**. 0.21 mmol of **14** afforded 0.16 mmol of **2** (76%): **mp** 129-130 ºC (hexane: $CHCl_3$); spectroscopic data agreed with those previously reported.[18,19]

**Dimethoxychalepensin (21):** **21** was prepared from **20**, the procedure differed slightly from the general above described. In the preparation of **21** the reaction mixture was heated for 2 days. 0.08 mmol of **20** afforded 0.05 mmol of **21** (63%): oil; **IR** (film) 2927, 2859, 1742, 1710, 1564, 1489, 1231, 1022, 801 $cm^{-1}$; **UV** (MeOH) $\lambda_{max}$ 326, 274, 263, 240, 220 nm; **$^1$H-NMR** ($CDCl_3$) $\partial$ 7.79 (s, 1H, H-4), 7.56 (d, 1H, J=2.1 Hz, H-2'), 7.05 (d, 1H, J=2.1 Hz, H-3'), 5.88 (dd, 1H, J=17.6 Hz and J=10.6 Hz, H-2"), 5.02 (d, 1H, J=17.6 Hz, trans H-3"), 5.00 (d, 1H, J=10.6 Hz, cis H-3"), 4.10 (s, 3H, -OMe), 3.99 (s, 3H, -OMe), 1.61 (s, 6H, C-1"-Me); **EIMS** m/z 314 (21), 299 (11), 286(11), 236 (20), 97 (56), 83 (61), 69 (44), 57 (100).

**3-(1,1-Dimethylallyl)seselin (22):** **22** was obtained from **28** following the same procedure as described for **21**.

0.10 mmol of **28** afforded 0.05 mmol of **22** (50%): melting point and spectroscopic data agreed with those given in the literature.[11]

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