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TETRAHEDRON

SILVER(I)/CELITE PROMOTED OXIDATIVE CYCLOADDITION OF 4-HYDROXYCOUMARIN TO OLEFINS. A FACILE SYNTHESIS OF DIHYDROFUROCOUMARINS AND FUROCOUMARINS

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Abstract: An efficient synthesis of dihydrofurocoumarins and furocoumarins is achieved from 4- hydroxycoumarins and olefins in the presence of Ag_2CO_3/Celite in moderate yields. The new method has been applied to the synthesis of the natural cyclobrachycoumarin isolated from Brachyclados megalanthus. © 1998 Elsevier Science Ltd. All rights reserved.

Dihydrofurocoumarin derivatives are widely distributed in nature (Figure 1).[2] They are reported to have various biological activities such as anticoagulant, insecticidal, anthelminthic, hypnotic, antifungal, phytoalexin, and HIV protease inhibition.[3] This wide range of biological properties has stimulated interest in the synthetic methods for the construction of dihydrofurocoumarins and furocoumarins. Although there are currently a number of methods available for the synthesis of dihydrofurocoumarins and furocoumarins, simple and efficient synthetic approaches are still scarce.[4]

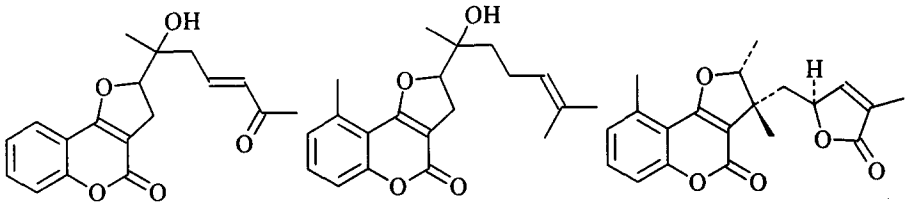

Figure 1

Oxidative radical cyclization mediated by metal salts (Mn(III), Ce(IV), and Co(II)) has become an important method in the synthesis of heterocycles.[5] We have been interested in oxidative radical cycloaddition of 1,3-dicarbonyl compounds to alkenes. In a previous communication, we have reported that silver(I)/Celite is a simple and convenient reagent for synthesis of dihydrofurans and furans.[6] We describe here the efficient synthesis of dihydrofurocoumarins and furocoumarins starting from 4-hydroxycoumarins and a variety of olefins such as alkenes, vinyl ether, dihydrofuran, dihydropyran, and vinyl sulfide utilizing Ag_2CO_3/Celite (Fetizon reagent).

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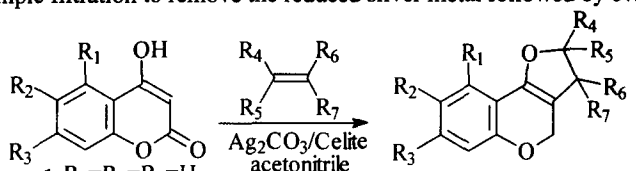
The sequence that we have developed begins with the reaction of 4-hydroxycoumarin with olefins (3-fold excess) in acetonitrile (Scheme 1). Two equivalents of Ag_2CO_3/Celite are used for the formation of the dihydrofurocoumarins. The course of the reaction can be readily monitored by TLC. Isolation of products involves a very simple filtration to remove the reduced silver metal followed by evaporation of the solvent.

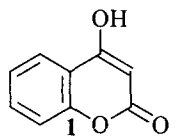
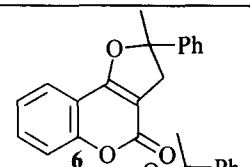
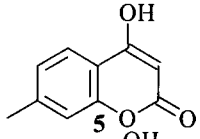
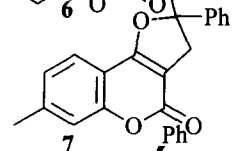
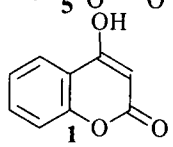
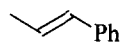
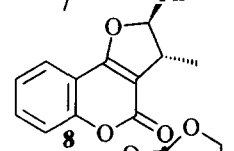
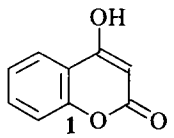
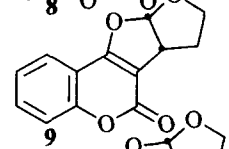
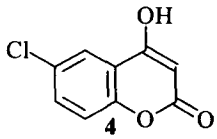
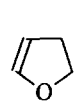
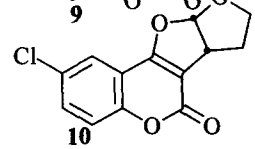


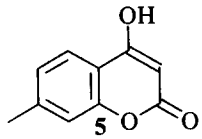
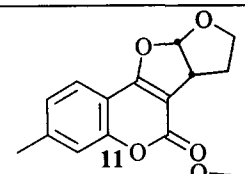
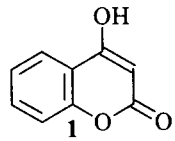
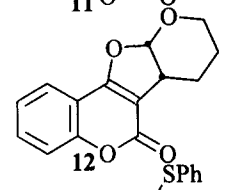
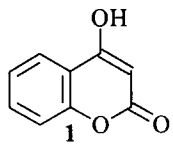
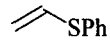
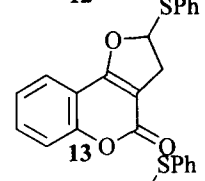
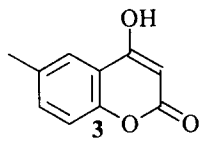
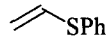
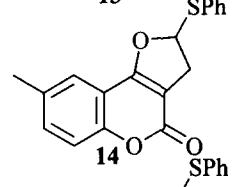
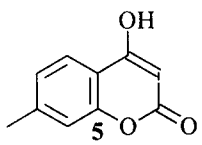
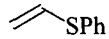
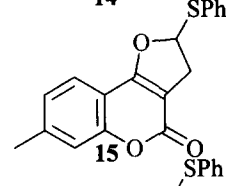
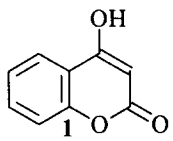
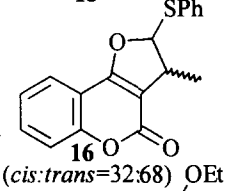
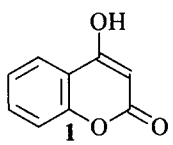
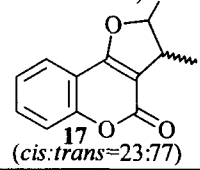
1 $R_1=R_2=R_3=H$
2 $R_1=CH_3$, $R_2=R_3=H$
3 $R_1=R_3=H$, $R_2=CH_3$
4 $R_1=R_3=H$, $R_2=Cl$
5 $R_1=R_2=H$, $R_3=CH_3$

Scheme 1

Reaction of 4-hydroxycoumarin **1** with α-methylstyrene in refluxing acetonitrile for 3 h gave dihydrofurocoumarin **6** in 37 % yield (Table 1, entry 1). The formation of dihydrofurocoumarin **6** is identified from its ^1H NMR absorption of methyl group as a singlet at δ 1.90. Similar results are summerized in Table 1. In the case of entries 1-10, only a single product was seen and no regio- and stereoisomers were found. The *trans*-stereochemistry of **8** is observed by the chemical shift (δ 1.55) of methyl group in ^1H NMR spectrum; the methyl group in *cis* isomer of the known 2,3-dihydro-3-methyl-2-phenylbenzofuran is shielded by the phenyl group and resonates at δ 0.81 as compared with δ 1.43 in the *trans* isomer.[7] On the other hand, reactions of several 4-hydroxycoumarins with dihydrofuran and dihydropyran afforded the fused acetals **9-12** in 25-58 % yields. The structures of **9-12** are clearly assigned as *cis*-compounds by analysis of the vicinal coupling constant of the two methine protons and by the analogy with earlier reported paper.[8] The acetal

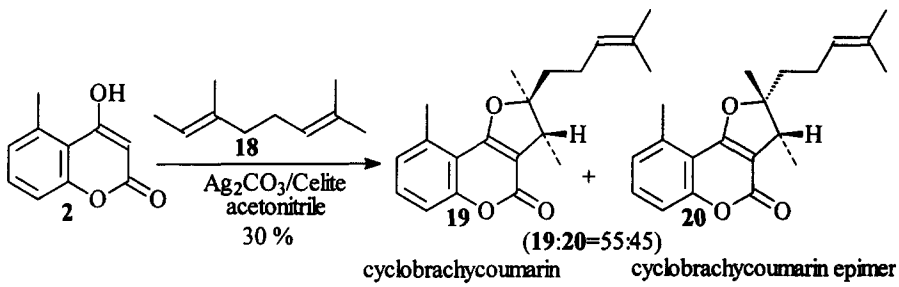
Table 1. Synthesis of Dihydrofurocoumarins

entry	4-hydroxycoumarin	olefin	dihydrofurocoumarin	yield (%)
1	 **1**		 **6**	37
2	 **5**		 **7**	43
3	 **1**		 **8**	30
4	 **1**		 **9**	40
5	 **4**		 **10**	42

entry	4-hydroxycoumarin	olefin	dihydrofurocoumarin	yield (%)
6				58
7				25
8				32
9				51
10				56
11		 (*cis:trans*=62:38)	 (*cis:trans*=32:68)	37
12		 (*cis:trans*=30:70)	 (*cis:trans*=23:77)	66

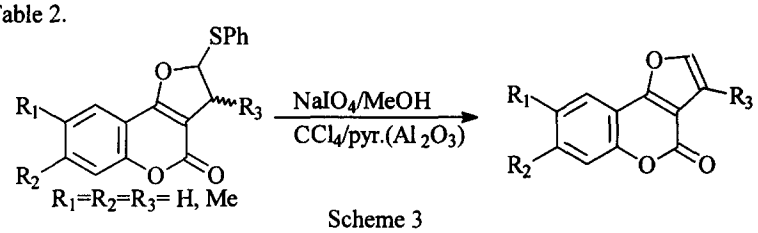
methine proton of **9** appeared as a doublet (J= 5.8 Hz) at δ 6.58 and that of **12** as a doublet (J= 7.6 Hz) at δ 6.29. In entries 11-12, both the *cis* and *trans* products were obtained. The stereochemical assignment of *cis*- and *trans*-isomers was easily defined by observation of the coupling constants between the vicinal protons.

Next, the one-step synthesis of cyclobrachycoumarin **19** isolated from the roots of the Argentinian Compositae *Brachyclados megalanthus* demonstrates an interesting application of this methodology.[9] Reaction of 5-methyl-4-hydroxycoumarin **2** with olefin **18** in refluxing acetonitrile for 3 h in the presence of Ag_2CO_3/Celite gave cyclobrachycoumarin **19** together with its epimer **20** as a 55 : 45 ratio in 30 % yield. The ratio is calculated from ^1H NMR spectrum of an inseparable mixture; the vinyl proton of **19** appeared at δ 5.07 and that of **20** at δ 5.19. The spectroscopic properties of our synthetic cyclobrachycoumarin **19** agreed well with those reported in the literature.[9]



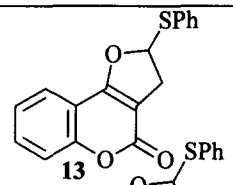
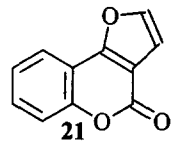
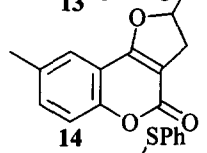
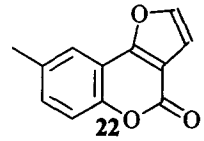
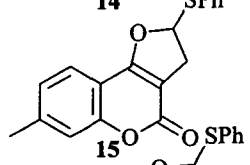
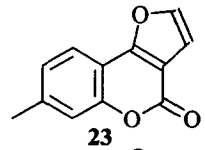
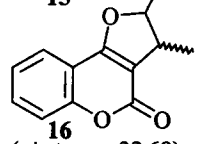
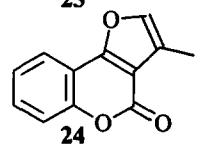
Scheme 2

Finally, the conversion of dihydrofurocoumarins to furocoumarins was investigated as shown in Scheme 3. The dihydrofurocoumarins **13-15** were treated with sodium periodate in aqueous methanol at room temperature for 24 h to form the corresponding sulfoxides, which on refluxing for 2 h with pyridine in carbon tetrachloride directly deliver the furocoumarins **21-23** in good yields (Table 2). The structures of the synthesized furocoumarins **21-23** are easily identified by the chemical shift of the vinylic proton in the furan ring. Both stereoisomers of *cis* and *trans* dihydrofurocoumarin **16** also were transformed into furocoumarin **24** in 71 % yield (Table 2, entry 4); although, active alumina had to be added in the elimination step to cause epimerization of the *cis*-sulfoxide prior to *syn*-elimination of the sulphenic acid.[10] The results are also collected in Table 2.

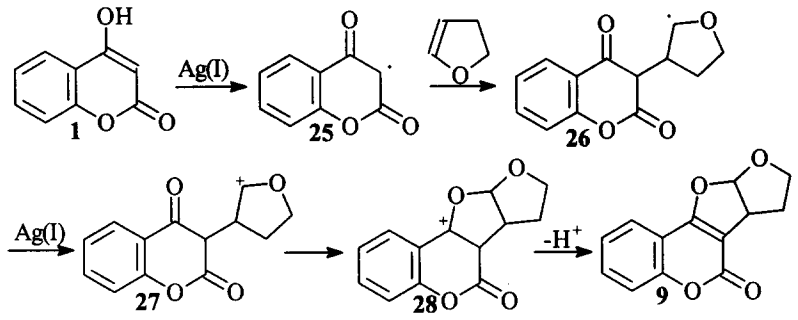


Scheme 3

Table 2. Synthesis of furocoumarins

entry	dihydrofurocoumarin	furocoumarin	yield (%)
1	 **13**	 **21**	82
2	 **14**	 **22**	79
3	 **15**	 **23**	82
4	 **16** (*cis*:*trans*=32:68)	 **24**	71

Although the exact mechanism of the reaction is still not clear, it is best described as shown in Scheme 4. The 4-hydroxycoumarin **1** is first oxidized by one equiv. of Ag(I) to generate the α-oxoalkyl radical **25**, which then attacks dihydrofuran to give the radical **26**. The adduct **26** now undergoes fast oxidation by one equiv. of Ag(I) to a carbocation **27**. Cyclization of the cation **27** furnishes intermediate **28**, which finally undergoes elimination to give the dihydrofurocoumarin **9**.



Scheme 4

In summary, a new synthesis of dihydrofurocoumarins and furocoumarins by silver(I)/Celite mediated oxidative cycloaddition of 4-hydroxycoumarins to olefins such as alkenes, vinyl ether, dihydrofuran, dihydropyran, and vinyl sulfide is described. The new method has been also applied to the synthesis of the natural cyclobrachycoumarin from *Brachyclados megalanthus.*

Experimental

All experiments were carried out under a nitrogen atmosphere. Merck precoated silica gel plates (Art. 5554) with fluorescent indicator were used for analytical TLC. Flash column chromatography was performed using silica gel 9385 (Merck). Melting points were determined with microcover glasses on a Fisher-Johns apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker Model ARX (300 MHz) spectrometer. IR spectra were recorded on a JASCO FTIR 5300 spectrophotometer. High resolution mass (HRMS) spectra were obtained VG-MICROMASS Autospec spectrometer.

General Procedure for Synthesis of the Dihydrofurocoumarins

To a heterogeneous solution of silver(I) carbonate (2.2 mmol, 50 wt % on Celite) in acetonitrile (20 mL) was added 4-hydroxycoumarin (1 mmol) and olefin (3 mmol) at room temperature. The reaction mixture was refluxed for 3 h and then cooled to room temperature. The suspension was filtered off and the inorganic material was washed with ethyl acetate (50 mL) and evaporated under reduced pressure to give the residue. The residue was purified by flash column chromatography on silica gel to give the dihydrofurocoumarin.

2-Methyl-2-phenyl-3,4-dihydro-2*H*-furo[3,2-*c*]chromen-4-one (6)

Reaction of 4-hydroxycoumarin **1** (162 mg, 1 mmol) with α-methylstyrene (354 mg, 3 mmol) in acetonitrile (20 mL) afforded **6** (103 mg, 37 %) as a solid: mp105 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (1H, dd, J= 7.8, 1.6 Hz), 7.59 (1H, m), 7.48-7.28 (7H, m), 3.39 (2H, q, J= 15.0 Hz), 1.90 (3H, s); IR (KBr) 3062, 2979, 1722, 1645, 1608, 1570, 1498, 1411, 1374, 1345, 1248, 1214, 1108, 1029, 752, 730, 700 cm^{-1}.

2,7-Dimethyl-2-phenyl-3,4-dihydro-2*H*-furo[3,2-*c*]chromen-4-one (7)

Reaction of 4-hydroxy-7-methylcoumarin **5** (176 mg, 1 mmol) with α-methylstyrene (354 mg, 3 mmol) in acetonitrile (20 mL) afforded **7** (125 mg, 43 %) as a solid: mp 146-147 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (1H, d, J= 8.0 Hz), 7.47-7.13 (7H, m), 3.37 (2H, q, J= 15.1 Hz), 2.48 (3H, s), 1.89 (3H, s); IR (KBr) 3049, 2986, 1718, 1649, 1622, 1518, 1410, 1346, 1273, 1062, 1035, 970, 893, 817, 773, 752, 709 cm^{-1}; HRMS m/z (M^+) calcd for $C_{19}H_{16}O_3$: 292.1099. Found: 292.1095.

3-Methyl-2-phenyl-3,4-dihydro-2*H*-furo[3,2-*c*]chromen-4-one (8)

Reaction of 4-hydroxycoumarin **1** (162 mg, 1 mmol) with *trans*-β-methylstyrene (354 mg, 3 mmol) in acetonitrile (20 mL) afforded **8** (82 mg, 30 %) as a solid: mp 73 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (1H, dd, J= 7.8, 1.6 Hz), 7.58 (1H, m), 7.44-7.30 (7H, m), 5.48 (1H, d, J= 7.3 Hz), 3.59 (1H, m), 1.55 (3H, d, J= 6.8Hz); IR (KBr) 3127, 1718, 1647, 1606, 1498, 1454, 1412,1238, 1207, 1157, 1099, 983, 941, 893, 754, 698 cm^{-1}.

6b,7,8,9a-Tetrahydro-6*H*-furo[3',2':4,5]furo[3,2-*c*]chromen-6-one (9)

Reaction of 4-hydroxycoumarin **1** (162 mg, 1 mmol) with dihydrofuran (350 mg, 5 mmol) in acetonitrile (20 mL) afforded **9** (93 mg, 40 %) as a solid: mp 139-140 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (1H, d, J= 7.9 Hz), 7.59 (1H, t, J= 8.4 Hz), 7.38 (1H, d, J= 8.3 Hz), 7.31(1H, t, J= 8.0 Hz), 6.58 (1H, d, J= 5.8 Hz), 4.22 (1H, m), 4.07 (1H, m), 3.75 (1H, m), 2.34 (1H, m), 2.21 (1H, m); IR (KBr) 3063, 2989, 1707, 1639, 1604, 1568, 1500, 1417, 1358, 1248, 1203, 1182, 1076, 1045, 1030, 1005, 943, 914, 885, 862, 802, 760 cm^{-1}; HRMS m/z (M^+) calcd for $C_{13}H_{10}O_4$: 230.0579. Found: 230.0596.

2-Chloro-6b,7,8,9a-tetrahydro-6*H*-furo[3',2':4,5]furo[3,2-*c*]chromen-6-one (10)

Reaction of 6-chloro-4-hydroxycoumarin **4** (197 mg, 1 mmol) with dihydrofuran (350 mg, 5 mmol) in acetonitrile (20 mL) afforded **10** (110 mg, 42 %) as a solid: mp 202-205 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (1H, d, J= 2.5 Hz), 7.52 (1H, dd, J= 8.8, 2.4 Hz), 7.32 (1H, d, J= 8.9 Hz), 6.59 (1H, d, J= 5.8 Hz), 4.22 (1H, m), 4.07 (1H, m), 3.73 (1H, m), 2.32 (1H, m), 2.22 (1H, m); IR (KBr) 3074, 2999, 1739, 1647, 1564, 1489, 1427, 1396, 1263, 1244, 1205, 1097, 1047, 1006, 974, 943, 862, 823, 788 cm^{-1}; HRMS m/z (M^+) calcd for $C_{13}H_9O_4Cl$: 264.0190. Found: 264.0186.

3-Methyl-6b,7,8,9a-tetrahydro-6*H*-furo[3',2':4,5]furo[3,2-*c*]chromen-6-one (11)

Reaction of 7-methyl-4-hydroxycoumarin **5** (176 mg, 1 mmol) with dihydrofuran (350 mg, 5 mmol) in acetonitrile (20 mL) afforded **11** (142 mg, 58 %) as a solid: mp 167-168 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (1H, d, J= 8.0 Hz), 7.16 (1H, s), 7.10 (1H, d, J= 8.0 Hz), 6.54 (1H, d, J= 5.8 Hz), 4.18 (1H, m), 4.03 (1H, m), 3.72 (1H, m), 2.44 (3H, s), 2.31(1H, m), 2.19 (1H, m); IR (KBr) 3057, 2991, 2947, 2885, 1726, 1641, 1618, 1556, 1514, 1423, 1236, 1327, 1265, 1093, 1076, 1045, 997, 945, 912, 862, 823, 796cm^{-1}; HRMS m/z (M^+) calcd for $C_{14}H_{12}O_4$: 244.0735. Found: 244.0758.

6,6b,7,8,9,10a-Hexahydropyrano[3',2':4,5]furo[3,2-*c*]chromen-6-one (12)

Reaction of 4-hydroxycoumarin **1** (162 mg, 1 mmol) with dihydropyran (420 mg, 5 mmol) in acetonitrile (20 mL) afforded **12** (61 mg, 25 %) as a solid: mp 124-126 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (1H, dd, J= 7.8, 1.4 Hz), 7.59 (1H, t, J= 8.5 Hz), 7.39 (1H, d, J= 8.4 Hz), 7.32 (1H, t, J= 7.8 Hz), 6.29 (1H, d, J= 7.6 Hz), 3.87 (2H, m), 3.49 (1H, m), 2.05 (2H, m), 1.81 (1H, m); 1.63 (1H, m); IR (KBr) 3086, 2951, 1705, 1637, 1604, 1566, 1500, 1452, 1398, 1271, 1219, 1140, 1074, 1026, 979, 898, 827, 765 cm^{-1}; HRMS m/z (M^+) calcd for $C_{14}H_{12}O_4$: 244.0735. Found: 244.0727.

2-[Phenylsulfanyl]-3,4-dihydro-2*H*-furo[3,2-*c*]chromen-4-one (13)

Reaction of 4-hydroxycoumarin **1** (162 mg, 1 mmol) with vinyl sulfide (408 mg, 3 mmol) in acetonitrile (20 mL) afforded **13** (95 mg, 32 %) as a solid: mp 125-126 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (1H, d, J= 7.8 Hz), 7.60-7.52 (3H, m), 7.39-7.28 (5H, m), 6.39 (1H, dd, J= 9.8, 6.1 Hz), 3.64 (1H, dd, J= 16.4, 9.8 Hz), 3.16 (1H, dd, J= 16.4, 6.2 Hz); IR (KBr) 3061, 2926, 1724, 1649, 1608, 1570, 1498, 1440, 1410, 1344, 1325, 1269, 1207, 1157, 1091, 1028, 941, 895, 860, 752, 731,692 cm^{-1}.

8-Methyl-2-[phenylsulfanyl]-3,4-dihydro-2*H*-furo[3,2-*c*]chromen-4-one (14)

Reaction of 6-methyl-4-hydroxycoumarin **3** (176 mg, 1 mmol) with vinyl sulfide (408 mg, 3 mmol) in acetonitrile (20 mL) afforded **14** (158 mg, 51 %) as a solid: mp 109-110 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58-7.54 (2H, m), 7.44 (1H, s), 7.37-7.26 (5H, m), 6.37(1H, dd, J= 9.8, 6.3 Hz), 3.61(1H, dd, J= 16.4, 9.8 Hz), 3.13 (1H, dd, J= 16.4, 6.3 Hz), 2.41 (3H, s); IR (KBr) 3076, 2982, 1714, 1649, 1610, 1577, 1494, 1439,

1394, 1271, 1203, 1095, 1035, 1006, 914, 858, 829, 798, 733, 690cm^{-1}; HRMS m/z (M^+) calcd for $C_{18}H_{14}O_3S$: 310.0663. Found: 310.0691.

7-Methyl-2-(phenylsulfanyl)-3,4-dihydro-2*H*-furo[3,2-*c*]chromen-4-one (15)

Reaction of 7-methyl-4-hydroxycoumarin **5** (176 mg, 1 mmol) with vinyl sulfide (408 mg, 3 mmol) in acetonitrile (20 mL) afforded **15** (174 mg, 56 %) as a solid: mp 157 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58-7.53 (3H, m), 7.34-7.32 (3H, m), 7.16 (1H, s), 7.09 (1H, d, J= 7.8 Hz), 6.35 (1H, dd, J= 9.8, 6.2 Hz), 3.60 (1H, dd, J= 16.3, 9.8 Hz), 3.12 (1H, dd, J= 16.3, 6.2 Hz), 2.45 (3H, s); IR (KBr) 3055, 1728, 1651, 1616, 1560, 1514, 1417, 1329, 1267, 1159, 1097, 1030, 993, 951, 864, 819, 754, 690 cm^{-1}; HRMS m/z (M^+) calcd for $C_{18}H_{14}O_3S$: 310.0663. Found: 310.0699.

3-Methyl-2-(phenylsulfanyl)-3,4-dihydro-2*H*-furo[3,2-*c*]chromen-4-one (16)

Reaction of 4-hydroxycoumarin **1** (162 mg, 1 mmol) with phenyl propenyl sulfide (450 mg, 3 mmol) in acetonitrile (20 mL) afforded **16** (115 mg, 37 %) as a 32: 68 ratio of *cis/trans* mixture; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71-7.55 (4H, m), 7.41-7.30 (5H, m), 6.41 (*cis*, 0.32H, d, J= 8.9 Hz), 5.86 (*trans*, 0.68H, d, J= 5.8 Hz), 3.93 (*cis*, 0.32H, m), 3.50 (*trans*, 0.68 H, m), 1.56 (cis, 0.96 H, d, J= 7.1 Hz), 1.50 (*trans*, 2.04 H, d, J=6.9 Hz); IR (KBr) 3061, 2972, 1722, 1649, 1606, 1498, 1408, 1325, 1269, 1157, 1095, 1064, 1028, 978, 891, 864, 754, 690 cm^{-1}.

2-Ethoxy-3-methyl-3,4- dihydro-2H-furo[3,2-c]chromen-4-one (17)

Reaction of 4-hydroxycoumarin **1** (162 mg, 1 mmol) with ethyl propenyl ether (430 mg, 5 mmol) in acetonitrile (20 mL) afforded **17** (162 mg, 66 %) as a 23: 77 ratio of *cis/trans* mixture: mp 80-81 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62 (1H, d, J= 7.7 Hz), 7.49 (1H, d, J= 8.5 Hz), 7.31 (1H, d, J= 8.3 Hz), 7.22 (1H, d, J= 7.6 Hz), 5.91 (*cis*, 0.23H, d, J= 7.3 Hz) and 5.52 (*trans*, 0.77H, d, J= 2.6 Hz), 3.95 (1H, m), 3.69 (1H, m), 3.51 (*cis*, 0.23H, m) and 3.28 (*trans*, 0.77H, m), 1.32 (3H, d, J= 7.2 Hz), 1.24 (3H, m); IR (KBr) 3067, 2980, 2935, 1720, 1647, 1570, 1501, 1454, 1412, 1379, 1348, 1271, 1246, 1207, 1119, 1059, 1030, 978 cm^{-1}; HRMS m/z (M^+) calcd for $C_{14}H_{14}O_4$: 246.0892. Found: 246.0897.

Cyclobrachycoumarin (19)

Reaction of 5-methyl-4-hydroxycoumarin **2** (176 mg, 1 mmol) with trans-2,6-dimethylocta-2,6-diene (414 mg, 3 mmol) in acetonitrile (20 mL) afforded cyclobrachycoumarin **19** and its epimer **20** as a 55 : 45 ratio (92 mg, 30 %) of an inseparable mixture: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 (1H, t, J= 7.8 Hz), 7.18 (1H, d, J= 8.3 Hz), 7.01 (1H, d, J= 7.5 Hz), 5.19 (0.45 H, m), 5.07 (0.55H, m), 3.24(1H, q, J=7.0 Hz), 2.65(3H, s), 2.12 (2H, m), 1.74 (2H, m), 1.63 (3H, s), 1.57 (3H, s), 1.45 (3H, s), 1.30 (3H, d, J= 7.1 Hz); IR(neat) 2972, 2926, 1724, 1630, 1564, 1516, 1450, 1383, 1329, 1240, 1170, 1070, 972, 829 cm^{-1}.

General Procedure for Synthesis of the Furocoumarins

To a solution of dihydrofurocoumarin (0.6-0.9 mmol) and water (5 mL) in methanol (10 mL) was added sodium periodate (1.2-1.8 mmol). The reaction mixture was stirred for 24 h at room temperature. After 24 h, water (10 mL) was added and the solution was extracted with dichloromethane (3 x 25 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated in vacuo to give the crude sulfoxide. To a solution of the crude sulfoxide in carbon tetrachloride (10 mL) was added pyridine (0.5 mL) and alumina (50 mg) at room temperature, and the mixture was refluxed for 2 h. Evaporation and purification by silica gel chromatography with 10 % ethyl acetate in hexane as an eluent afforded the furocoumarin.

4*H*-Furo[3,2-*c*]chromen-4-one (21)

Reaction of dihydrofurocoumarin **13** (210 mg, 0.7 mmol) with sodium periodate (300 mg, 1.4 mmol) in aqueous methanol and *syn*-elimination in refluxing carbon tetrachloride (10 mL) with pyridine (0.5mL) afforded **21** (108 mg, 82 %) as a solid: mp 97-98 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (1H, d, J= 8.1 Hz), 7.65 (1H, d, J= 2.0 Hz), 7.53 (1H, t, J= 8.3 Hz), 7.45 (1H, d, J= 7.8 Hz), 7.36 (1H, t, J= 7.9 Hz), 7.01

(1H, d, J= 2.0 Hz); IR (KBr) 3150, 3126, 1736, 1633, 1597, 1564, 1498, 1448, 1431, 1356, 1317, 1296, 1122, 1084, 1060, 856, 787, 752 cm^{-1}; HRMS m/z (M^+) calcd for $C_{11}H_6O_3$: 186.0317. Found: 186.0301.

7-Methyl-4*H*-furo[3,2-*c*]chromen-4-one (22)

Reaction of dihydrofurocoumarin **14** (200 mg, 0.6 mmol) with sodium periodate (280 mg, 1.2 mmol) in aqueous methanol and *syn*-elimination in refluxing carbon tetrachloride (10 mL) with pyridine (0.5 mL) afforded **22** (102 mg, 79 %) as a solid: mp 152-153 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.65 (1H, s), 7.61 (1H, d, J= 2.0 Hz), 7.34-7.31(2H, m), 6.98 (1H, d, J= 2.1 Hz), 2.44 (3H, s); IR (KBr) 3126, 1722, 1637, 1572, 1506, 1442, 1385, 1130, 1093, 981, 908, 814, 752 cm^{-1}.

6-Methyl-4*H*-furo[3,2-*c*]chromen-4-one (23)

Reaction of dihydrofurocoumarin **15** (200 mg, 0.6 mmol) with sodium periodate (280 mg, 1.2 mmol) in aqueous methanol and *syn*-elimination in refluxing carbon tetrachloride (10 mL) with pyridine (0.5 mL) afforded **23** (106 mg, 82 %) as a solid: mp 148-149 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.54 (1H, d, J= 8.2 Hz), 7.59 (1H, d, J= 2.1 Hz), 7.24 (1H, s), 7.16 (1H, d, J= 8.3 Hz), 6.97 (1H, d, J= 2.0 Hz), 2.46 (3H, s); IR (KBr) 3157, 3123, 1730, 1633, 1556, 1500,1448, 1319, 1290, 1269, 1161, 1145, 1095, 1055, 966, 941, 889, 869, 812, 748, 684, 667 cm^{-1}; HRMS m/z (M^+) calcd for $C_{12}H_8O_3$: 200.0473. Found: 200.0487.

3-Methyl-4*H*-furo[3,2-*c*]chromen-4-one (24)

Reaction of dihydrofurocoumarin **16** (290 mg, 0.9 mmol) with sodium periodate (400 mg, 1.8 mmol) in aqueous methanol and *syn*-elimination in refluxing carbon tetrachloride (10 mL) with pyridine (0.5 mL) and alumina (50 mg) afforded **24** (132 mg, 71 %) as a solid: mp 152-153 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.85 (1H, d, J= 7.8, Hz), 7.53-7.40 (2H, m), 7.41 (1H, s), 7.33 (1H, t, J= 7.8 Hz), 2.37 (3H, s); IR (KBr) 3146, 2959, 1749, 1633, 1581, 1502, 1446, 1419, 1388, 1192, 1145, 1095, 889, 783, 750 cm^{-1}; HRMS m/z (M^+) calcd for $C_{12}H_8O_3$: 200.0473. Found: 200.0462.

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