Atom Economy. Palladium Catalyzed Formation of Coumarins by Additions of Phenols and Alkynoates via a net C-H Insertion.

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Supplementary Material

5,7-Dimethoxy-4-phenylcoumarin **6a**

Using *method A*, 3,5-dimethoxyphenol (50 mg, 0.32 mmol), palladium acetate (13.5 mg, 0.06 mmol), sodium acetate (10 mg, 0.12 mmol) and alkynoate **5a** (72 mg, 0.42 mmol) were reacted in formic acid (3 mL) at 35º C for 16h. Flash chromatography eluting with methylene chloride, and recrystallization from methylene chloride:hexanes afforded **6a** (72 mg, 69 %) as a white solid, mp 164-165º C (lit mp.[44] 165-166º C). IR(film): 2925, 1713, 1614, 1595, 1460, 1353, 1160, 1111 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.36 (m, 3H), 7.25 (m, 2H), 6.51 (d, *J* = 2.0 Hz, 1H), 6.21 (d, *J* = 2.0 Hz, 1H), 5.99 (s, 1H), 3.85 (s, 3H), 3.40 (s, 3H). ^{13}C-NMR (125 MHz, $CDCl_3$): δ 163.3, 160.9, 158.2, 157.2, 155.7, 139.7, 127.9, 127.3, 127.1, 112.7, 103.5, 95.7, 93.5, 55.8, 55.4.

5,7-Dimethoxy-4-methylcoumarin **6b**

Using *method A*, 3,5-dimethoxyphenol (50 mg, 0.32 mmol), palladium acetate (13.5 mg, 0.06 mmol), sodium acetate (10 mg, 0.12 mmol) and butynoate **5b** (75 µL, 0.64 mmol) were reacted in formic acid (3 mL) at 50º C for 14h. The usual workup afforded **6b** (44mg, 51%).

Using *method B*, 3,5-dimethoxyphenol (200 mg, 1.30 mmol), Pd_2dba_3•$CHCl_3$ (33 mg, 0.032 mmol), sodium acetate (11 mg, 0.13 mmol) and alkynoate **5b** (180 µL, 1.56 mmol) were reacted in formic acid (1.5 mL) at room temperature for 16h. Flash chromatography eluting methylene chloride, followed by recrystallization from methanol afforded **6b** (217 mg, 63%) as a white solid, mp 168-170º C (lit mp.[6a] 172-3º C). IR (film): 2933, 1726, 1608, 1473, 1455, 1353, 1154, 1112 cm^{-1}.^{1}H-NMR (300 MHz, $CDCl_3$): δ 6.33 (d, *J* = 2.5 Hz, 1H), 6.18 (d, *J* = 2.5 Hz, 1H), 5.96 (s, 1H), 3.75 (s, 3H), 3.74 (s, 3H), 2.43 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 163.1, 161.3, 159.5, 157.2, 154.7, 111.5, 105.1, 95.5, 93.7, 56.0, 55.9, 24.7.

5,7-Dimethoxy-4-([2'-ethoxycarbonyloxy]ethyl)coumarin **6c**

Using *method A*, 3,5-dimethoxyphenol (25 mg, 0.16 mmol), palladium acetate (3.5 mg, 0.016 mmol) and alkynoate **5c** (64 mg, 0.3 mmol) were reacted in formic acid (0.2 mL) at room temperature for 16h. The usual workup affords **6c** (24mg, 41%).

Using *method B*, 3,5-dimethoxyphenol (200 mg, 1.29 mmol), Pd_2dba_3•$CHCl_3$ (33 mg, 0.032 mmol) and alkynoate **5c** (550 mg, 2.59 mmol) were reacted in formic acid (1.2 mL) at room temperature for 16h. Flash chromatography eluting with 30% benzene:pentanes afforded **6c** (275 mg, 58%) as a white solid, mp 112-5º C. IR(film): 2982, 2849, 1744, 1615, 1466, 1386, 1353, 1260, 1159, 1115 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$): 6.45 (d, *J* = 2.3 Hz, 1H), 6.30 (d, *J* =2.3 Hz, 1H), 6.00 (s, 1H), 4.38 (t, *J* = 6.4 Hz, 2H), 4.16 (q, *J* = 7.0 Hz, 2H), 3.87 (s, 3H), 3.84 (s, 3H), 3.26 (t, *J* = 6.4 Hz, 2H), 1.29 (t, *J* = 7.0 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$): 162.9, 160.6, 158.3, 157.3, 155.0, 128.3,112.6, 103.7, 95.6, 93.7, 66.1, 64.1, 55.9, 55.7, 35.7, 14.2. HRMS Calc'd for $C_{16}H_{18}O_7$: 322.1053. Found: 322.1047.

5,7-Dimethoxy-4-(3'-cyanopropyl)coumarin **6d**

Using *method B*, 3,5-dimethoxyphenol (38 mg, 1.30 mmol), Pd_2dba_3•$CHCl_3$ (6.5 mg, 0.006 mmol), and alkynoate **5d** (75 mg, 0.50 mmol) were reacted in formic acid (0.3 mL) at room temperature for 12h. Flash chromatography eluting with 1:1 ether:pentanes afforded **6d** (45 mg, 66%) as a tan solid. IR(film): 2926, 2849, 2247, 1720, 1614, 1456, 1208, 1157, 1114 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 6.48 (d, *J* = 2.2 Hz, 1H), 6.33 (d, *J* = 2.2 Hz, 1H), 5.99 (s, 1H), 3.93 (s, 3H), 3.86 (s, 3H), 3.06 (t, *J* = 6.8 Hz, 2H), 2.47 (t, *J* = 6.8 Hz, 2H), 1.96 (p, *J* = 7.0 Hz, 2H). ^{13}C-NMR (125 MHz, $CDCl_3$): δ 163.0, 158.2, 157.5, 155.5, 131.5, 119.3, 111.6, 103.6, 95.8, 93.8, 56.0, 55.8, 35.4, 26.4, 17.1. HRMS Calc'd for $C_{15}H_{15}NO_4$: 273.1001. Found: 273.1010.

5,6,7-Trimethoxycoumarin (fraxinol methyl ether) **8**

Using *method B*, 3,4,5-trimethoxyphenol **7** (200 mg, 1.09 mmol), Pd_2dba_3•$CHCl_3$ (28 mg, 0.027 mmol), sodium acetate (9 mg, 0.11 mmol) and ethyl propynoate **2** (220 µL, 2.17 mmol) were reacted in formic acid (1.0 mL) at room temperature for 16h. Flash chromatography eluting with 30% ethyl acetate:hexanes followed by recrystallization from methanol afforded **8** (141 mg, 46%) as a light yellow solid, mp 72-4º C (lit.[45b] mp 74-5º C). IR(film): 2940, 2854, 1732, 1610, 1465, 1381, 1263, 1140, 1110 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.90 (d, *J* = 9.7 Hz, 1H), 6.56 (s, 1H), 6.18 (d, *J* = 9.7 Hz, 1H), 3.98 (s, 3H), 3.87 (s, 3H), 3.81 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 161.8, 157.1, 151.4, 149.2, 138.8, 138.0, 112.3, 107.1, 95.4, 61.7, 61.1, 56.2.

7-Methoxycoumarin (herniarin) **14a** and 5-methoxycoumarin **15a**

Using *method A*, 3-methoxyphenol (130 mg, 1.06 mmol), palladium acetate (24 mg, 0.016 mmol) and ethyl propynoate **2** (210 µL, 2.11 mmol) were reacted in formic acid

(0.2 mL) at 50º C for 16h. After the usual workup, flash chromatography eluting with 95:5 methylene chloride:diethyl ether afforded **14a** (122 mg, 52%) and **15a** (17 mg, 7%). Using *method B*, 3-methoxyphenol (250 mg, 1.60 mmol), Pd_2dba_3•$CHCl_3$ (41 mg, 0.04 mmol), sodium acetate (14 mg, 0.16 mmol) and ethyl propynoate **2** (320 µL, 3.20 mmol) were reacted in formic acid (2.0 mL) at room temperature for 18h. Flash chromatography eluting 20% ethyl acetate:hexanes afforded **14a** (179 mg, 44%) and **15a** (33mg, 8%). **14a**, mp 119-120º C (lit.[14c,d] mp 118º C). IR(film): 2922, 2851, 1732, 1614, 1464, 1282, 1232, 1121, 1028 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.64 (d, *J* = 9.6 Hz, 1H), 7.38 (d, *J* = 8.5 Hz, 1H), 6.84 (m, 2H), 6.25 (d, *J* = 9.6 Hz, 1H), 3.88 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 163.2, 161.4, 156.5, 143.4, 128.8, 113.6, 112.7, 112.6, 101.1, 55.9. **15a**, mp 80-2º C (lit.[17a] mp 81-2º C). IR(film): 2981, 1732, 1614, 1464, 1282, 1242, 1121, 1028 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.05 (d, *J* = 9.6 Hz, 1H), 7.38 (t, *J* = 8.4 Hz, 1H), 6.82 (d, *J* = 8.4 Hz, 1H), 6.62 (d, *J* = 8.4 Hz, 1H), 6.33 (d, *J* = 9.6 Hz, 1H), 3.89 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 163.2, 161.4, 156.5, 143.4, 128.8, 113.6, 112.7, 112.6, 101.1, 55.9.

<u>7-Methoxy-5-methylcoumarin **14b** and 5-methoxy-7-methylcoumarin **15b**</u>

Using *method B*, 3-methoxy-5-methylphenol **13b** (100 mg, 0.64 mmol), Pd_2dba_3•$CHCl_3$ (17 mg, 0.016 mmol), sodium acetate (5 mg, 0.064 mmol) and ethyl propynoate **2** (130 µL, 1.30 mmol) were reacted in formic acid (0.7 mL) at room temperature for 14h. Flash chromatography eluting methylene chloride afforded **14b** (184 mg, 72%) and **15b** (25 mg, 10%). **14b**, mp 139-142º C (lit. mp[19a] 142-3). IR(film): 2923, 2850, 1735, 1606, 1459, 1301, 1239, 1149, 1120, 1047 cm^{-1}. ^{1}H-NMR (500 MHz, CDCl3): δ 7.81 (d, *J* = 9.8 Hz, 1H), 6.66 (d, *J* = 2 Hz, 1H), 6.64 (d, *J* = 2 Hz, 1H), 6.23 (d, *J* = 9.8 Hz, 1H), 3.83 (s, 3H), 2.45 (s, 3H). ^{13}C-NMR (125 MHz, $CDCl_3$): δ 162.3, 161.5, 156.5, 140.5, 137.2, 113.9, 112.3, 111.6, 98.6, 55.6, 18.5. **15b**, mp 117-9º C (lit.[19a] mp119-120). IR(film): 2922, 1720, 1619, 1445, 1390, 1239, 1118, 1024 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 8.02 (d, *J* = 9.8 Hz, 1H), 6.72 (s, 1H), 6.50 (s, 1H), 6.24 (d, *J* = 9.8 Hz, 1H), 3.89 (s, 3H), 2.41 (s, 3H). ^{13}C-NMR (125 MHz, $CDCl_3$): δ 165.1, 161.3, 155.1, 143.8, 138.6, 113.3, 109.5, 106.3, 93.1, 55.9, 22.4.

<u>7-Hydroxy-5-methoxycoumarin **17a** and 5-hydroxy-7-methoxycoumarin **18a**</u>

Using *method B*, 5-methoxyresorcinol **16** (50 mg, 0.36 mmol), Pd_2dba_3•$CHCl_3$ (9 mg, 0.09 mmol) and ethyl propynoate **2** (70 µL, 0.80 mmol) were reacted in formic acid (0.4 mL) at room temperature for 16h. Flash chromatography eluting with 10% ethyl acetate:benzene afforded **17a** (30 mg, 39%) and **18a** (24 mg, 32%). **17a**, mp 139-142º C (lit.[18a] mp 142-3). IR(film): 3253, 2850, 1735, 1606, 1459, 1301, 1239, 1149, 1120, 1047 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$ + DMSO-d_6): δ 7.96 (d, *J* = 9.8 Hz, 1H), 6.34 (s, d, *J*

= 2.0 Hz, 1H), 6.31 (d, *J* = 2.0 Hz, 1H), 6.00 (d, *J* = 9.8 Hz, 1H), 3.85 (s, 3H). **18a**, mp 117-9º C (lit.[18a] mp119-120). IR(film): 3242, 1720, 1619, 1445, 1390, 1239, 1118, 1024 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$ +DMSO-d_6): δ 8.01 (d, *J* = 9.8 Hz, 1H), 6.36 (d, *J* = 2.0 Hz, 1H), 6.28 (d, *J* = 2.0 Hz, 1H), 6.03 (d, *J* = 9.8 Hz, 1H), 3.83 (s, 3H).

7-Hydroxy-5-methoxy-4-methylcoumarin **17b** and 5-hydroxy-7-methoxy-4-methylcoumarin **18b**

Using *method B*, 5-methoxyresorcinol **16** (50 mg, 0.36 mmol), Pd_2dba_3•$CHCl_3$ (9 mg, 0.09 mmol) and ethyl butynoate **5b** (83 μL, 0.71 mmol) were reacted in formic acid (0.4 mL) at room temperature for 16h. Flash chromatography eluting with 10% ethyl acetate:benzene afforded **17b** (27 mg, 34%) and **18b** (22 mg, 28%). **17b**, mp 261-2º C (lit.[18c] mp 257-8º C). IR(film): 3268, 1725, 1606, 1459, 1362, 1149, 1120, 1047 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$ + DMSO-d_6): δ 6.37 (d, *J* = 2.4 Hz, 1H), 6.29 (d, *J* = 2.4 Hz, 1H), 5.94 (q, *J* = 1.0 Hz, 1H), 3.82 (s, 3H), 2.85 (br s, 1H) 2.40 (d, *J* = 1.0 Hz, 3H). **18b**, mp 256-7º C (lit.[18c] mp 224-5º C). IR(film): 3242, 1723, 1614, 1432, 1349, 1157 1118, 1027 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$ + DMSO-d_6): δ 6.33 (d, *J* = 2.4 Hz, 1H), 6.27 (d, *J* = 2.4 Hz, 1H), 5.96 (q, *J* = 1.0 Hz, 1H), 3.78 (s, 3H), 2.82 (br s, 1H), 2.46 (d, *J* = 1.0 Hz, 3H).

4-([3'-ethoxycarbonyloxy]propyl)-7-hydroxy-5-methoxycoumarin **17h** and 4-([3'-ethoxycarbonyloxy]propyl)-7-hydroxy-5-methoxycoumarin **18h**

Using *method B*, 5-methoxyresorcinol (100 mg, 0.71 mmol), Pd_2dba_3•$CHCl_3$ (19 mg, 0.018 mmol) and alkynoate **5h** (325 mg, 1.43 mmol) were reacted in formic acid (1.2 mL) at room temperature for 6h. After 6h, additional **5h** (65 mg, 0.29 mmol) was added and the reaction mixture stirred at room temperature for 18h. The reaction mixture was diluted with water (5 mL), extracted with methylene chloride (3 x 5 mL) and the combined organic extracts dried ($MgSO_4$) and concentrated *in vacuo*. Flash chromatography eluting with 2% methanol:methylene chloride afforded **17h** (75 mg, 33%) and **18h** (33 mg, 14%). **17h**, mp 210-3º C. IR(film): 3420, 2983, 1741, 1723, 1620, 1600, 1472, 1366, 1265, 1162, 1113, 1026 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$ + DMSO-d_6): δ 9.71 (s, 1H), 6.40 (d, *J* = 2.0 Hz, 1H), 6.22 (d, *J* = 2.0 Hz, 1H), 5.84 (s, 1H), 4.15-4.1 (m, 4H), 3.78 (s, 3H), 3.26 (t, *J* = 6.8 Hz, 2H), 1.89 (m, 2H), 1.25 (t, *J* = 7.4 Hz, 3H). ^{13}C-NMR (125 MHz, $CDCl_3$ + DMSO-d_6): δ 177.5 161.3, 158.6, 157.0, 156.9, 155.0, 110.0, 102.7, 96.5, 95.8, 66.9, 63.8, 55.5, 32.8, 38.6, 14.1. Anal. Calc'd for $C_{16}H_{18}O_7$: C, 59.62; H, 5.63. Found C, 59.74; H, 5.73. **18h**, mp 194-8º C. IR(film): 3348, 2923, 1743, 1728, 1602, 1464, 1259, 1156, 1113, 1087 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 6.34 (d, *J* = 2.0 Hz, 1H), 6.24 (d, *J* = 2.0 Hz, 1H), 5.91 (s, 1H),

4.15-4.05 (m, 4H), 3.72 (s, 3H), 2.95 (t, *J* = 7.0 Hz, 2H), 1.98 (m, 2H), 1.71 (br s, 1H),1.21 (t, *J* = 7.5 Hz, 3H). HRMS Calc'd for $C_{16}H_{18}O_7$: 322.1053. Found: 322.1059

5,6-Benzocoumarin **20**

Using a modification of *method B*, a solution β-naphthol **19** (100 mg, 0.69 mmol), Pd_2dba_3•$CHCl_3$ (18 mg, 0.017 mmol), sodium acetate (6 mg, 0.07 mmol) and ethyl propynoate **2** (130 μL, 1.30 mmol) in formic acid (0.7 mL) was sonicated at room temperature for 3h. After the typical workup, flash chromatography eluting with methylene chloride and recrystallization from ethanol afforded **20** (102 mg, 61%) as a yellow solid, mp 109-112º C (lit.[48] mp 116-117º C). IR(KBr): 2998, 1738, 1636, 1563, 1439, 1259, 1120, 1023, 824 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 8.50 (d, *J* = 10.1 Hz, 1H), 8.21 (d, *J* = 8.5 Hz, 1H), 8.00 (d, *J* = 9.1 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.73 (dd, *J* = 8.5 and 7.0 Hz, 1H), 7.56 (dd, *J* = 8.0 and 7.0 Hz, 1H), 7.47 (d, *J* = 9.1 Hz, 1H), 6.61 (d, *J* = 10.1 Hz, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$): δ 160.3, 153.5, 138.5, 133.5, 130.8, 128.9, 128.1, 127.9, 125.6, 120.9, 116.5, 114.9, 111.9.

8-Bromo-5,7-dimethoxycoumarin **22**

Using *method A*, 2-Bromo-3,5-dimethoxyphenol **21**[26] (100 mg, 0.43 mmol), palladium acetate (10 mg, 0.046 mmol) and ethyl propynoate **2** (85 μL, 0.46 mmol) were reacted in formic acid (0.4 mL) at 35º C for 12h. After the usual workup, flash chromatography eluting with 20% diethyl ether:pentanes affords **3** (64 mg, 52%) and **23** (24 mg, 12%). IR(film): 1723, 1609, 1345, 1241, 1225, 1120, 1100, 821 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$ + dmso-d_6): 7.92 (d, *J* = 9.8 Hz, 1H), 6.31 (s, 1H), 6.13 (d, *J* = 9.8 Hz, 1H), 3.95 (s, 3H), 3.91 (s, 3H). ^{13}C-NMR (125 MHz, $CDCl_3$+ dmso-d_6): 163.9, 160.4, 159.9, 156.2, 138.4, 111.4, 104.5, 90.9, 56.7, 56.1. HRMS Calc'd for $C_{11}H_9BrO_4$: 283.9660. Found: 283.9690.

E-2-(2'-Benzenesulfonylethenyl)-3,5-dimethoxyphenol **24**

Using *method A*, 3,5-dimethoxyphenol **1** (50 mg, 0.32 mmol), palladium acetate (7 mg, 0.03 mmol), sodium acetate (5 mg, 0.06 mmol) and ethynyl sulfonylbenzene **23a**[27] (108 mg, 0.65 mmol) were reacted in formic acid (3 mL) at 35º C for 17h. Flash chromatography eluting with 50% ethyl acetate:hexanes afforded **24** (19 mg, 18%) as a white solid, mp 178-180º C. IR(film): 3333, 2919, 2850, 1599, 1462, 1278, 1158, 1136, 1098, 1081 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$ + acetone-d_6): δ 8.83 (s, 1H), 7.90 (d, *J* = 15.3 Hz, 1H), 7.72 (dd, *J* = 8.8 and 1.0 Hz, 2H), 7.37 (td, *J* = 7.4 and 1.0 Hz, 1H), 7.31 (m, 2H), 7.05 (d, *J* = 15.3 Hz, 1H), 5.94 (d, *J* = 1.9 Hz, 1H), 5.82 (d, *J* = 1.9 Hz, 1H), 3.64 (s, 3H), 3.58 (s, 3H). ^{13}C-NMR (75 MHz, acetone-d_6): δ 160.5, 162.8, 160.8., 144.1, 133.5, 132.1, 128.1, 128.6, 126.9,, 103.5, 93.3, 90.2, 55.3, 54.9. HRMS Calc'd for $C_{16}H_{16}O_5S$: 320.0718. Found: 320.0716.

General procedure of silver(I) mediated reactions.

To a clear solution of **1** (50 mg, 0.32 mmol) and silver tetrafluoroborate (63 mg, 0.32 mmol) in dry THF (0.5 mL) was added ethyl propynoate (66 μL, 0.65 mmol) and the resulting yellow solution stirred at room temperature for 4 h. The reaction mixture was diluted with pentanes, and the precipitated silver salts removed by filtration through a short pad of silica and washing with 1:1 diethyl ether:pentanes. The filtrate was concentrated *in vacuo* and the solid recrystallized from methylene chloride:pentanes to afford **3** (75 mg, 92%) as a white solid. (see above for characterization data of **3**).

5,7-Dihydroxy-2,2-dimethylchroman-4-one **29**

Phloroglucinol (28.0 g, 0.22 mol) and dimethylacrylic acid (22.3 g, 0.22 mol) were slowly added into phosphorus oxychloride (100 mL), forming a dark orange solution. To the reaction mixture was added zinc chloride (93.3g, 0.40 mmol) and the resulting red solution stirred at room temperature for 18h. The reaction mixture is then cautiously poured onto crushed ice (2L) and the resulting orange precipitate collected by suction filtration and dried in a vacuum oven overnight at 100º C to afford **29** as an orange solid (22.7g, 60%), mp 198-200º C (lit.[53] mp 198º C). IR(KBr): 3150, 2995, 1641, 1578, 1502, 1336, 1302, 1170, 1086 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 5.91 (d, *J* = 2.2 Hz, 1H), 5.85 (d, *J* = 2.2 Hz, 1H), 5.60 (br s, 2H), 2.67 (s, 2H), 1.43 (s, 6H). ^{13}C-NMR (75 MHz, acetone-d_6): δ 196.9, 167.3, 165.0, 162.7, 102.4, 96.2, 96.1, 47.8, 26.7.

2,2-Dimethyl-7-hydroxy-5-methoxychromene **30**

A 250 round-bottom flask, fitted with a condenser, containing potassium carbonate (25 g, 180 mmol), chroman-4-one **29** (5.4 g, 26 mmol) and *p*-toluenesulfonyl chloride (4.9 g, 26 mmol) was charged with acetone (90 mL) and the resulting clear yellow solution heated at 60º C. After 5h, the solution was treated with additional potassium carbonate (11g, 78 mmol) followed by iodomethane (2.0 mL, 30 mmol) and heating at 60º C continued for an additional 16 h. The reaction mixture was cooled to room temperature, filtered to remove potassium salts and the filtrate concentrated *in vacuo*. The resulting yellow foam was recrystallized from methylene choloride:hexanes to afford 5-methoxy-7-tosyloxychromanone (8.1 g, 83% yield) as a white solid, mp 150-1º C (lit.[37b] mp 152º C). IR(film): 2977, 1691, 1596, 1420, 1379, 1178, 1117, 1017 cm^{-1} ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.73 (d, *J* = 8.8 Hz, 2H), 7.31 (d, *J* = 8.8 Hz, 2H), 6.21 (d, *J* = 2.0 Hz, 1H), 6.05 (d, *J* = 2.0 Hz, 1H), 3.71 (s, 3H), 2.60 (s, 2H), 2.42 (s, 3H), 1.36 (s, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 190.2, 162.2, 161.1, 154.9, 145.7, 132.1, 129.8, 128.4, 109.0, 104.0, 97.9 79.3, 56.2, 49.9, 26.3, 21.7.

To a solution of the tosyl protected chroman-4-one (1.0 g, 2.66 mmol) in THF (90 mL) was added 1.0M borane•THF (3.2 mL, 3.2 mmol) and the resulting turbid white solution stirred at room temperature for 12h. After 12h, the solution is treated with 1M sodium bisulfate (25 mL) and stirred at room temperature for 1h. The reaction mixture was extracted with diethyl ether (2 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Flash chromatography eluting with 1:1 diethyl ether:pentanes, followed by recrystallization from methanol, afforded the tosyl protected chromene (650 mg, 68% yield) as colorless plates, mp 98-9º C (lit.[37b] mp 98º C). IR(film): 2974, 1622, 1587, 1479, 1379, 1178, 1117, 1017 cm^{-1} ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.75 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 6.56 (d, *J* = 10.0 Hz, 1H), 6.12 (d, *J* = 2.0 Hz, 1H), 6.02 (d, *J* = 2.0 Hz, 1H), 5.52 (d, *J* = 10.0 Hz, 1H), 3.70 (s, 3H), 2.45 (s, 3H), 1.36 (s, 6H).

To a solution of 5-methoxy-7-tosyloxychromene (630 mg, 1.75 mmol) in ethanol (25 mL) was added a solution of KOH (1.4 g, 24.5 mmol) in water (25 mL). The resulting orange solution was heated at 80° C. After 1h, the orange solution was cooled to room temperature, acidified with 1M sodium bisulfate and extracted with ether (3 x 25 mL). The combined ether extracts were washed with 10% sodium bicarbonate (25 mL), brine (25 mL), dried ($MgSO_4$), concentrated *in vacuo* and recrystallized from ether:hexanes to afford **30** (209 mg, 58 %) as a faint yellow solid, mp 103-4º C (lit.[38b] mp 104º C). IR(film): 3350, 1620, 1505, 1477, 1160, 1120, 835 cm^{-1} ^{1}H-NMR (300 MHz, $CDCl_3$): δ 6.54 (d, *J* = 10.2 Hz, 1H), 5.94 (d, *J* = 2.0 Hz, 1H), 5.92 (d, *J* = 2.0 Hz, 1H), 5.41 (d, *J* = 10.2 Hz, 1H), 4.83 (s, 1H), 3.75 (s, 3H), 1.38 (s, 6H).

2,2-Dimethyl-7-hydroxy-5-methoxychroman **31**

To a suspension of zinc powder (1.74 g, 26.6 mmol) and 5-methoxy-7-tosyloxychrom-4-one (1.0 g, 2.7 mmol) in ethanol (25 mL), at 0º C, was cautiously added (dropwise) concentrated hydrochloric acid (4 mL). Once the addition of the acid was complete the resulting clear yellow solution was stirred at room temperature for 3h then extracted with diethyl ether (3 x 25 mL). The combined ether extracts were washed with 1N sodium hydroxide (25 mL), brine (25 mL), dried ($MgSO_4$), and concentrated *in vacuo* to afford (671 mg, 70%) as slightly yellow foam. IR(film): 2975, 2938, 1599, 1371, 1192, 1179, 1012, 963 cm^{-1} ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.74 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 6.08 (d, *J* = 2.2 Hz, 1H), 6.03 (d, *J* = 2.2 Hz, 1H), 3.68 (s, 3H), 2.54 (t, *J* = 6.8 Hz, 2H), 2.44 (s, 3H), 1.71 (t, *J* = 6.8 Hz, 2H), 1.25 (s, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 159.6, 156.4, 150.4, 146.7, 131.4, 131.3, 130.1, 110.3, 105.5, 98.1, 76.1, 57.0, 33.3, 27.9, 23.1, 18.3.

To a solution of tosyl protected chromanone (620 mg, 1.72 mmol) in ethanol (20 mL) was added a solution of potassium hydroxide (1.35 g, 24 mmol) in water (20 mL). The resulting orange solution was heated at 80° C. After 5h, the orange solution was cooled to room temperature, acidified with 1M sodium bisulfate and the turbid solution extracted with ether (3 x 25 mL). The combined ether extracts were washed with brine (25 mL), dried ($MgSO_4$), concentrated *in vacuo* and recrystallized from ether:hexanes to afford **31** (347 mg, 98%) as a light yellow solid, mp 101-3° C (lit.[38b] mp 104-5° C). IR(film): 3485, 2974, 2938, 1606, 1454, 1418, 1157, 1112, 1083 cm^{-1} ^{1}H-NMR (300 MHz, $CDCl_3$): δ 5.98 (d, *J* = 2.4 Hz, 1H), 5.92 (d, *J* = 2.2 Hz, 1H), 5.00 (s, 1H), 3.77 (s, 3H), 2.54 (t, *J* = 6.8 Hz, 2H), 1.74 (t, *J* = 6.8 Hz, 2H), 1.30 (s, 6H).

5,7-Dihydroxy-2,2-dimethylchroman **32**

To a suspension of zinc powder (9.0 g, 140 mmol) and chroman-4-one **29** (3.0 g, 14 mmol) in methanol (50 mL), at 0° C, was cautiously added (dropwise) concentrated hydrochloric acid (20 mL). Once the addition of the acid was complete, the resulting clear yellow solution was stirred at room temperature for 2h, diluted with brine (25 mL) and extracted with diethyl ether (3 x 25 mL). The combined ether extracts were washed with brine (25 mL), dried ($MgSO_4$), and concentrated *in vacuo* to afford **32** (671 mg, 70%) as slightly yellow foam which was generally used without further purification. Recrystallization from benzene afforded pale yellow plates, mp 160-163° C (lit.[40] mp 162-163). IR(film): 3481, 2967, 2936, 1632, 1607, 1515, 1459, 1149, 1048, 1005 cm^{-1} ^{1}H-NMR (300 MHz, $CDCl_3$): δ 5.92 (s, 2H), 5.20 (br s, 2H), 2.56 (t, *J* = 6.7 Hz, 2H), 1.78 (t, *J* = 6.7 Hz, 2H), 1.31 (s, 6H).