Syntheses of Naturally Occurring 5-Carbonylmethyl-7-hydroxy-2-methyl-chromones and -chromanone (Studies on the β -Carbonyl Compounds Connected with the β -Polyketides. X)¹⁾

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Naturally occurring 5-carbonylmethyl-7-hydroxy-2-methyl-chromones, -chromanone and an analogue 1, 2, 3, and 4 were synthesized by two routes from a self condensation product 6 of dimethyl acetonedicarboxylate, and the pyrone 10.

Keywords chromone; chromanone; natural product; synthesis; condensation reaction; β -ketide

Several 5-carbonylmethyl-7-hydroxy-2-methyl-chromones and a -chromanone, namely, 5-carboxymethyl-7-hydroxy-2-methylchromone (**1**),²⁾ 5-carboxymethyl-7-hydroxy-2-methylchromanone (**2**),²⁾ aloesone,³⁾ aloesol,²⁾ 5-acetonyl-7-hydroxy-2-methylchromone (**3**),^{2,4,5)} barakol (**4**),⁶⁾ etc., are known among the naturally occurring 2,5-dialkyl-chromones, -chromanones and their analogues from plants. Compounds **1**, **2**, and **3** are constituents of rhubarb (used as a crude drug in China, commercial name: Bateidaio, 馬蹄大黃),²⁾ and compounds **3** and **4** are constituents of *Cassia siamea* BRITT. (used as a crude drug in Thailand: cassod tree, Thai copper pod).^{4–6)}

Although a biomimetic synthesis⁷⁾ and another synthesis⁶⁾ of the chromone **3** (a precursor for the synthesis and biosynthesis of barakol (**4**)) had been established, we wished to develop a general synthesis of the naturally occurring chromones and chromanone **1–4** in connection with the medicinal uses of their parent plants.

The synthetic strategies consist of the use of β -ketide condensation reactions such as the reaction of dimethyl acetonedicarboxylate to form a product **6**, and the reaction of the pyrone **10** with acetylacetone to form the chromone **11**, as shown in Chart 1.

The starting material **6** was synthesized by the self condensation reaction of dimethyl 3-oxoglutarate in the presence of potassium fluoride in a yield of 61.1% and transformed to **12** (59.2% yield) by treatment with concentrated H_2SO_4 . The Pechmann condensation reaction of **7**, **12**, and **13** with ethyl acetoacetate for the construction of the chromone nucleus according to Hirata and Suga⁸⁾ was unsuccessful under various conditions. On the other hand,

the 2-acetyl compound **14** was easily obtained by the acetylation of **7**, prepared by the methylation of **12**, with acetyl chloride in the presence of boron trifluoride etherate in a yield of 82.6%.

Thus, the constructions of chromone and chromanone nuclei for the syntheses of natural products from **7** were accomplished in the following way. Acylation of **7** with tetrolyl chloride⁹⁾ in the presence of boron trifluoride etherate afforded **8** (46.6% yield) followed by treatment with H_2SO_4 in AcOH and H_2O to give **1** (68.3%), which gave physical data identical with data reported for the natural product. On the other hand, reaction with **7** and crotonyl chloride in the presence of boron trifluoride etherate gave **16** (63.2% yield) followed by refluxing in CCl_4 to afford **9** (86.7% yield). Treatment of **9** with H_2SO_4 in AcOH and H_2O gave a chromanone **5** (69.1% yield, a racemate of the natural product **2**).

The key intermediate **11** for the second synthetic strategy was synthesized by the reaction of the pyranone **10**¹⁰⁾ with acetylacetone in the presence of sodium hydride and butyl lithium¹¹⁾ in a yield of 32.6%. The chromone **11** can also be synthesized from **1**. That is, treatment of **18**, prepared from **1** by methylation followed by hydrolysis, with Ac_2O gave **11** (42.4% yield), in which acylation and decarboxylation took place spontaneously.

Finally, demethylation of **11** by treatment with $AlCl_3$ in benzene afforded a natural chromone **3** (70.8% yield). Compound **3** can be transformed to **4** by treatment with concentrated H_2SO_4 as reported by Harris and Wittek.⁷⁾ All physical data of synthetic **3** were identical with those of the natural product.^{2,4,5)}

Chart 1

i, KF; ii, conc. H_2SO_4 ; iii, $\text{MeI}/\text{K}_2\text{CO}_3$; iv, CH_2N_2 or $\text{MeOH}/\text{conc. H}_2\text{SO}_4$; v, $\text{AcCl}/\text{BF}_3 \cdot \text{OEt}_2$; vi, $\text{Ac}_2\text{O}/\text{pyridine}$; vii, $\text{MeC}\equiv\text{CCOCl}/\text{BF}_3 \cdot \text{OEt}_2$; viii, conc. $\text{H}_2\text{SO}_4/\text{AcOH}/\text{H}_2\text{O}$; ix, $\text{MeCH}=\text{CHCOCl}/\text{BF}_3 \cdot \text{OEt}_2$; x, CCl_4 (reflux)

Chart 2

i, $\text{MeI}/\text{K}_2\text{CO}_3$; ii, conc. $\text{H}_2\text{SO}_4/\text{AcOH}/\text{H}_2\text{O}$; iii, Ac_2O (reflux); iv, AlCl_3 ; v, conc. H_2SO_4 ; vi, $(\text{CH}_2\text{OH})_2/\text{BF}_3 \cdot \text{OEt}_2$; vii, $\text{CH}_2(\text{Ac})_2/\text{NaH}/\text{LiBu}$

Chart 3

Experimental

All melting points are uncorrected. Infrared (IR) spectra were recorded with a Hitachi 260-10 spectrometer, nuclear magnetic resonance (NMR) spectra with a JEOL JNM-FX 100 spectrometer with tetramethylsilane as an internal standard, and mass spectra (MS) with a JEOL JMS-D 300 spectrometer. Elemental analyses were done by Ms. A. Sakamoto and Ms. T. Yoda, Kissei Pharmaceutical Company Ltd., Japan. Mallinckrodt silica gel (100 mesh) and Merck Kieselgel G nach Stahl were used for column chromatography and thin layer chromatography (TLC), respectively.

Methyl 3,5-Dihydroxy-2,4-bis(methoxycarbonyl)phenylacetate (6) Potassium fluoride (55.2 g) was added to a solution of dimethyl 3-oxoglutarate (42 g) in absolute toluene (600 ml), and the whole was refluxed with separation of water by means of a Dean-Stark trap. After refluxing for 24 h, the reaction mixture was concentrated under a vacuum, poured into ice-water, and then extracted with chloroform. The organic layer was washed with H_2O , then dried and concentrated. The residue was recrystallized from ether-hexane to yield 22 g (61.1%) of **6** as colorless needles, mp 131–133°C. IR (KBr) cm^{-1} : 3430, 1738, 1675, 1580. NMR (CDCl_3) δ : 3.70 (3H, s, $-\text{CO}_2\text{Me}$), 3.84 (2H, s, $-\text{CH}_2-$), 3.88 (3H, s, $-\text{CO}_2\text{Me}$), 4.03 (3H, s, $-\text{CO}_2\text{Me}$), 6.38 (1H, s, aromatic H), 11.90 (1H, s, $-\text{OH}$), 12.8 (1H, s, $-\text{OH}$). MS m/z Calcd for $\text{C}_{13}\text{H}_{14}\text{O}_7$ (M^+): 282.0738. Found: 282.0678. Anal. Calcd for $\text{C}_{13}\text{H}_{14}\text{O}_7$: C, 52.35; H, 4.73. Found: C, 52.22; H, 4.74.

4-Carboxy-3,5-dihydroxyphenylacetic Acid (12) A solution of **6** (10 g) in concentrated H_2SO_4 (50 ml) was heated overnight at 65°C with stirring

and the whole was poured into ice-water. The resulting solids were removed by filtration and the filtrate was extracted with ethyl acetate. The organic layer was washed with saturated NaCl, then dried and concentrated. The residue was recrystallized from chloroform-ethyl acetate to yield 4.2 g (59.2%) of **12** as colorless prisms, mp 198–200°C. IR (KBr) cm^{-1} : 3420, 1675, 1640, 1570, 1480. NMR (CDCl_3 - $\text{DMSO}-d_6$) δ : 3.46 (2H, s, $-\text{CH}_2-$), 6.40 (2H, s, aromatic H), 8.30 (4H, s, $2 \times -\text{OH}$, $2 \times -\text{CO}_2\text{H}$). MS m/z Calcd for $\text{C}_9\text{H}_8\text{O}_6$ (M^+): 212.0318. Found: 212.0272. Anal. Calcd for $\text{C}_9\text{H}_8\text{O}_6$: C, 50.95; H, 3.80. Found: C, 50.77; H, 3.81.

Methyl 3,5-Dimethoxy-4-methoxycarbonylphenylacetate (13) Methyl iodide (0.5 ml) and anhydrous K_2CO_3 (200 mg) were added to a solution of **12** (50 mg) in N,N -dimethylformamide (DMF, 2 ml) and the whole was stirred overnight at room temperature. The reaction mixture was poured into ice-water and extracted with ethyl acetate. The organic layer was washed with saturated NaHCO_3 and saturated NaCl, then dried and concentrated. The residue was subjected to silica gel chromatography. The chloroform eluate gave 51.6 mg (83.2%) of **13** as colorless prisms, mp 75.5–77°C. IR (Nujol) cm^{-1} : 1720, 1600, 1580. NMR (CDCl_3) δ : 3.63 (2H, s, $-\text{CH}_2-$), 3.73 (3H, s, $-\text{CO}_2\text{Me}$), 3.84 (6H, s, $2 \times -\text{OMe}$), 3.93 (3H, s, $-\text{CO}_2\text{Me}$), 6.53 (2H, s, aromatic H). MS m/z Calcd for $\text{C}_{13}\text{H}_{16}\text{O}_6$ (M^+): 268.0945. Found: 268.0930. Anal. Calcd for $\text{C}_{13}\text{H}_{16}\text{O}_6$: C, 58.20; H, 6.01. Found: C, 58.21; H, 6.13.

Methyl 3,5-Dihydroxy-4-methoxycarbonylphenylacetate (7) A large excess of an ether solution of diazomethane was added to a solution of **12** (200 mg) in methanol (10 ml) and the whole was kept at room temperature

for 10 min. The reaction mixture was concentrated and the residue was subjected to silica gel chromatography. The chloroform eluate gave 188 mg (83.0%) of **7** as colorless prisms (ether–hexane), mp 74–74.5 °C. IR (KBr) cm^{-1} : 3360, 1720, 1670, 1635, 1560. NMR (CDCl_3) δ : 3.60 (2H, s, $-\text{CH}_2-$), 3.80 (3H, s, $-\text{CO}_2\text{Me}$), 4.16 (3H, s, $-\text{CO}_2\text{Me}$), 6.46 (2H, s, aromatic H), 9.47 (2H, s, $2 \times -\text{OH}$). MS m/z Calcd for $\text{C}_{11}\text{H}_{12}\text{O}_6$ (M^+): 240.0635. Found: 240.0657. Anal. Calcd for $\text{C}_{11}\text{H}_{12}\text{O}_6$: C, 55.00; H, 5.04. Found: C, 55.06; H, 5.05.

Methyl 3,5-Dihydroxy-4-methoxycarbonylphenylacetate (7) Concentrated H_2SO_4 (0.5 gtt.) was added to a solution of **12** (50 mg) in methanol (1 ml) and the whole was refluxed for 4 h. The reaction mixture was concentrated and the residue was subjected to silica gel chromatography. The chloroform eluate gave 33 mg (66.0%) of **7** as colorless prisms (ether–hexane), mp 74–74.5 °C.

Methyl 2-Acetyl-3,5-dihydroxy-4-methoxycarbonylphenylacetate (14) Boron trifluoride etherate (18 ml) was added to a solution of **7** (1 g) in acetyl chloride (2.8 g) and the whole was heated overnight at 80 °C with stirring. The reaction mixture was poured into ice-water and extracted with ethyl acetate. The organic layer was washed with saturated NaHCO_3 and saturated NaCl, then dried and concentrated. The residue was subjected to silica gel chromatography. The chloroform eluate gave 0.97 g (82.6%) of **14** as colorless needles (ether–hexane), mp 99.5–101 °C. IR (Nujol) cm^{-1} : 3460, 1745, 1700, 1680, 1660, 1580. NMR (CDCl_3) δ : 2.78 (3H, s, $-\text{COMe}$), 3.70 (3H, s, $-\text{CO}_2\text{Me}$), 3.73 (2H, s, $-\text{CH}_2-$), 4.13 (3H, s, $-\text{CO}_2\text{Me}$), 6.42 (1H, s, aromatic H), 9.68 (1H, s, $-\text{OH}$), 10.67 (1H, s, $-\text{OH}$). MS m/z 282 (M^+). Anal. Calcd for $\text{C}_{13}\text{H}_{14}\text{O}_7$: C, 55.32; H, 5.00. Found: C, 55.54; H, 5.06.

Methyl 3,5-Diacetoxy-2-acetyl-4-methoxycarbonylphenylacetate (15) Acetic anhydride (3 ml) was added to a solution of **14** (230 mg) in dry pyridine (1 ml) and the whole was allowed to stand overnight at room temperature. The reaction mixture was poured into ice-water and extracted with chloroform. The organic layer was washed with saturated NaHCO_3 , dilute HCl, and H_2O , then dried and concentrated. The residue was recrystallized from ether–hexane to yield 252 mg (84.4%) of **15** as colorless prisms, mp 101–102 °C. IR (neat) cm^{-1} : 1775, 1740, 1700, 1620, 1565. NMR (CDCl_3) δ : 2.30 (6H, s, $2 \times -\text{OCOMe}$), 2.47 (3H, s, $-\text{COMe}$), 3.67 (3H, s, $-\text{CO}_2\text{Me}$), 3.75 (2H, s, $-\text{CH}_2-$), 3.84 (3H, s, $-\text{CO}_2\text{Me}$), 7.02 (1H, s, aromatic H). MS m/z 366 (M^+). Anal. Calcd for $\text{C}_{17}\text{H}_{18}\text{O}_9$: C, 55.74; H, 4.95. Found: C, 55.87; H, 5.02.

Methyl 2-Crotonyl-3,5-dihydroxy-4-methoxycarbonylphenylacetate (16) Boron trifluoride etherate (16 ml) was added to a solution of **7** (875 mg) in crotonyl chloride (3.2 g) and the whole was heated overnight at 80 °C with stirring. The reaction mixture was poured into ice-water and extracted with ethyl acetate. The organic layer was washed with saturated NaHCO_3 and H_2O , then dried and concentrated. The residue was subjected to silica gel chromatography. The chloroform eluate gave 710 mg (63.2%) of **16** as a colorless oil. IR (neat) cm^{-1} : 3430, 1740, 1670, 1640, 1580. NMR (CDCl_3) δ : 1.89 (3H, d, $J=6$ Hz, $-\text{Me}$), 3.57 (2H, s, $-\text{CH}_2-$), 3.65 (3H, s, $-\text{CO}_2\text{Me}$), 4.08 (3H, s, $-\text{CO}_2\text{Me}$), 6.50 (1H, s, aromatic H), 6.55 (1H, d, $J=6$ Hz, olefinic H), 6.59 (1H, m, olefinic H), 9.73 (1H, s, $-\text{OH}$), 10.33 (1H, s, $-\text{OH}$). MS m/z Calcd for $\text{C}_{15}\text{H}_{16}\text{O}_7$ (M^+): 308.0897. Found: 308.0914.

7-Hydroxy-8-methoxycarbonyl-5-methoxycarbonylmethyl-2-methyl-4-chromanone (9) A solution of **16** (30 mg) in carbon tetrachloride (2 ml) was refluxed overnight and then concentrated. The residue was recrystallized from ether–hexane to yield 26 mg (86.7%) of **9** as colorless prisms, mp 103.5–105 °C. IR (KBr) cm^{-1} : 1740, 1680, 1660, 1580. NMR (CDCl_3) δ : 1.53 (3H, d, $J=7$ Hz, $-\text{Me}$), 2.64 (2H, d, $J=8$ Hz, $-\text{CH}_2-$), 3.72 (3H, s, $-\text{CO}_2\text{Me}$), 3.98 (5H, s, $-\text{CH}_2-$, $-\text{CO}_2\text{Me}$), 4.53 (1H, m, methine H), 6.45 (1H, aromatic H), 12.14 (1H, br, $-\text{OH}$). MS m/z Calcd for $\text{C}_{15}\text{H}_{16}\text{O}_7$ (M^+): 308.0897. Found: 308.0922. Anal. Calcd for $\text{C}_{15}\text{H}_{16}\text{O}_7$: C, 58.44; H, 5.23. Found: C, 58.21; H, 5.28.

5-Carboxymethyl-7-hydroxy-2-methyl-4-chromanone (5) A solution of concentrated H_2SO_4 (3.5 ml) in H_2O (14 ml) was added to a solution of **9** (300 mg) in acetic acid (17 ml) and the whole was heated overnight at 100 °C with stirring. The reaction mixture was poured into ice-water and extracted with ethyl acetate. The organic layer was washed with H_2O , then dried and concentrated. The residue was subjected to silica gel chromatography. The eluate with 20% ethyl acetate in chloroform gave 160 mg (69.1%) of **5** as colorless prisms (ethyl acetate–chloroform), mp 207–208 °C. IR (KBr) cm^{-1} : 1710, 1645, 1610, 1590, 1570. NMR (CDCl_3 – $\text{DMSO}-d_6$) δ : 1.37 (3H, d, $J=6$ Hz, $-\text{Me}$), 2.54 (2H, m, $-\text{CH}_2-$), 3.79 (2H, s, $-\text{CH}_2-$), 4.45 (1H, m, methine H), 6.25 (1H, d, $J=2$ Hz, aromatic H), 6.29 (1H, d, $J=2$ Hz, aromatic H), 10.47 (1H, br, $-\text{OH}$), and 11.60 (1H, br, $-\text{CO}_2\text{H}$). MS m/z Calcd for $\text{C}_{12}\text{H}_{12}\text{O}_5$ (M^+): 236.0684. Found: 236.0669.

Anal. Calcd for $\text{C}_{12}\text{H}_{12}\text{O}_5$: C, 61.01; H, 5.12. Found: C, 60.21; H, 5.22.

7-Hydroxy-8-methoxycarbonyl-5-methoxycarbonylmethyl-2-methylchromone (8) Boron trifluoride etherate (29 ml) was added to a solution of **7** (1.6 g) in tetraolyl chloride⁹⁾ (6 g) and the whole was heated overnight at 80 °C with stirring. The reaction mixture was poured into ice-water and extracted with ethyl acetate. The organic layer was washed with saturated NaHCO_3 and saturated NaCl, then the mixture was stirred at room temperature for 1 h. The mixture was acidified with concentrated HCl and extracted with chloroform. The organic layer was washed with H_2O , then dried and concentrated. The residue was subjected to silica gel chromatography. The chloroform eluate gave 0.95 g (46.6%) of **8** as colorless needles (ether–hexane), mp 136–138 °C. IR (KBr) cm^{-1} : 3400, 1738, 1660, 1625, 1570. NMR (CDCl_3) δ : 2.35 (3H, s, $-\text{Me}$), 3.72 (3H, s, $-\text{CO}_2\text{Me}$), 4.03 (3H, s, $-\text{CO}_2\text{Me}$), 4.13 (2H, s, $-\text{CH}_2-$), 6.07 (1H, s, olefinic H), 6.77 (1H, s, aromatic H), 12.08 (1H, s, $-\text{OH}$). MS m/z Calcd for $\text{C}_{15}\text{H}_{14}\text{O}_7$ (M^+): 306.0739. Found: 306.0744. Anal. Calcd for $\text{C}_{15}\text{H}_{14}\text{O}_7$: C, 58.83; H, 4.61. Found: C, 58.79; H, 4.66.

5-Carboxymethyl-7-hydroxy-2-methylchromone (1) Concentrated H_2SO_4 (3 ml) and H_2O (2 ml) were added to a solution of **8** (50 mg) in acetic acid (2.5 ml) and the whole was heated overnight at 120 °C. The reaction mixture was made basic with Na_2CO_3 and heated at 60 °C for 1 h with stirring. The mixture was acidified with concentrated HCl and extracted with ethyl acetate. The organic layer was washed with H_2O , then dried and concentrated. The residue was recrystallized from methanol to yield 26 mg (68.3%) of **1** as colorless needles, mp 263–265 °C (lit.²⁾ mp 263–265 °C).

7-Methoxy-5-methoxycarbonylmethyl-2-methylchromone (17) Methyl iodide (1 ml) and anhydrous K_2CO_3 (400 mg) were added to a solution of **1** (100 mg) in DMF (4 ml) and the whole was stirred overnight at room temperature. The reaction mixture was poured into ice-water and extracted with chloroform. The organic layer was washed with dilute HCl and H_2O , then dried and concentrated. The residue was recrystallized from ether–hexane to yield 109 mg (96.5%) of **17** as colorless needles, mp 140–142 °C. IR (Nujol) cm^{-1} : 1725, 1665, 1610. NMR (CDCl_3) δ : 2.31 (3H, s, $-\text{Me}$), 3.72 (3H, s, $-\text{CO}_2\text{Me}$), 3.88 (3H, s, $-\text{OMe}$), 4.14 (2H, s, $-\text{CH}_2-$), 6.00 (1H, s, olefinic H), 6.77 (1H, d, $J=2$ Hz, aromatic H), 6.88 (1H, d, $J=2$ Hz, aromatic H). MS m/z Calcd for $\text{C}_{14}\text{H}_{14}\text{O}_5$ (M^+): 262.0839. Found: 262.0821. Anal. Calcd for $\text{C}_{14}\text{H}_{14}\text{O}_5$: C, 64.12; H, 5.38. Found: C, 63.83; H, 5.48.

5-Carboxymethyl-7-methoxy-2-methylchromone (18) Concentrated H_2SO_4 (3.6 ml) and H_2O (1.6 ml) were added to a solution of **17** (40 mg) in acetic acid (2 ml) and the whole was heated overnight at 100 °C. The reaction mixture was made basic with Na_2CO_3 , then kept at 60 °C for 1 h with stirring. The mixture was acidified with concentrated HCl, then extracted with ethyl acetate. The organic layer was washed with H_2O , then dried and concentrated. The residue was recrystallized from methanol to give 34 mg (89.7%) of **18** as colorless needles, mp 237–239 °C. IR (Nujol) cm^{-1} : 1730, 1632, 1616, 1585. NMR (CDCl_3 + $\text{DMSO}-d_6$) δ : 2.33 (3H, s, $-\text{Me}$), 2.92 (1H, br, $-\text{CO}_2\text{H}$), 3.89 (3H, s, $-\text{OMe}$), 4.13 (2H, s, $-\text{CH}_2-$), 6.02 (1H, s, olefinic H), 6.74 (1H, d, $J=2$ Hz, aromatic H), 6.80 (1H, d, $J=2$ Hz, aromatic H). MS m/z 248 (M^+). Anal. Calcd for $\text{C}_{13}\text{H}_{12}\text{O}_5$: C, 62.90; H, 4.89. Found: C, 62.65; H, 4.95.

5-Acetonil-7-methoxy-2-methylchromone (11) A solution of **18** (10 mg) in acetic anhydride (4 ml) was refluxed for 4 h with stirring. The reaction mixture was poured into ice-water and extracted with ethyl acetate. The organic layer was washed with H_2O , then dried and concentrated under a vacuum. The residue was subjected to silica gel chromatography. The chloroform eluate gave 4.2 mg (42.4%) of **11** as colorless platy crystals, mp 138–140 °C (ether–hexane). IR (KBr) cm^{-1} : 1715, 1653, 1603, 1565. NMR (CDCl_3) δ : 2.30 (3H, s, $-\text{Me}$), 2.37 (3H, s, $-\text{COMe}$), 3.86 (3H, s, $-\text{OMe}$), 4.20 (2H, s, $-\text{CH}_2-$), 5.96 (1H, s, olefinic H), 6.62 (1H, d, $J=2$ Hz, aromatic H), 6.75 (1H, d, $J=2$ Hz). MS m/z Calcd for $\text{C}_{14}\text{H}_{14}\text{O}_4$ (M^+): 246.0890. Found: 246.0884. Anal. Calcd for $\text{C}_{14}\text{H}_{14}\text{O}_4$: C, 68.28; H, 5.73. Found: C, 68.22; H, 5.73.

5-Acetonil-7-hydroxy-2-methylchromone (3) Anhydrous aluminum chloride (332 mg) was added to a solution of **11** (100 mg) in absolute benzene (3.3 ml) and the whole was refluxed for 75 min with stirring. The reaction mixture was concentrated under a vacuum, to 3 N HCl (7.5 ml) was added and the whole was stirred at 0 °C for 20 min, poured into ice-water and extracted with ethyl acetate. The organic layer was washed with H_2O , then dried and concentrated. The residue was recrystallized from ethyl acetate to yield 66.8 mg (70.8%) of **3** as colorless prisms, mp 214–216 °C (lit.²⁾ mp 214–216 °C).

6-(2,2-Ethylenediisopropyl)-4-methoxy-2H-2-pyrone (10) Ethylene glycol (0.1 ml) and boron trifluoride etherate (0.02 ml) were added to a

solution of **19**¹⁰) (50 mg) in chloroform (0.2 ml) and the whole was allowed to stand overnight at room temperature. The reaction mixture was poured into ice-water and extracted with chloroform. The organic layer was washed with H₂O, then dried and concentrated. The residue was recrystallized from ether-hexane to yield 58.7 mg (94.5%) of **10** as colorless prisms, mp 52–53 °C. IR (KBr) cm⁻¹: 1723, 1650, 1563. NMR (CDCl₃) δ : 1.40 (3H, s, -Me), 2.77 (2H, s, -CH₂-), 3.81 (3H, s, -OMe), 3.97 (4H, s, -CH₂CH₂-), 5.45 (1H, d, *J*=2 Hz, olefinic H), 5.95 (1H, d, *J*=2 Hz, olefinic H). MS *m/z* 226 (M⁺). Anal. Calcd for C₁₁H₁₄O₅: C, 58.40; H, 6.24. Found: C, 58.17; H, 6.47.

5-Acetyl-7-methoxy-2-methylchromone (11) Sodium hydride (55%, 96 mg) was added to a solution of acetylacetone (200 mg) in absolute tetrahydrofuran (5 ml) with stirring at 0 °C under a nitrogen atmosphere and the whole was stirred at 0 °C for 10 min. A solution of 1.6 M butyl lithium in hexane (1.2 ml) was added and the mixture was stirred at 0 °C for 10 min under the same conditions. Compound **10** (226 mg) was then added and the mixture was stirred at 0 °C for 20 min under the same conditions. The reaction mixture was poured into ice-water, acidified with 10% HCl, and extracted with ethyl acetate. The organic layer was washed with H₂O, then dried and concentrated. The residue was dissolved in acetone (8 ml), concentrated HCl (0.8 ml) was added, and the solution was allowed to stand overnight at room temperature. The solution was then made basic with saturated NaHCO₃ and extracted with ethyl acetate. The

organic layer was washed with H₂O, then dried and concentrated. The residue was subjected to silica gel chromatography. The chloroform eluate gave 80.2 mg (32.6%) of **11** as colorless platy crystals (ether-hexane), mp 138–140 °C.

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