Synthetic Studies on Naturally Occurring Coumarins. II. Synthesis of 6,7-Dimethoxy- and 7,8-Dimethoxy-5-[(*E*)-3-oxo-1-butenyl]coumarins

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In connection with studies on the structure elucidation of the so-called Reisch's coumarin isolated from *Toddalia asiatica*, syntheses of two coumarins (4 and 5) were accomplished *via* the routes shown in Charts 2 and 3, respectively. Melting points and NMR data of the synthesized coumarins (4 and 5) and of related coumarins (5-methoxysuberenon, toddalenone, and Reisch's coumarin) are given in Table I, suggesting that so-called Reisch's coumarin might be 4.

Keywords Reisch's coumarin; 5-methoxysuberenon; toddalenone; Claisen rearrangement; aryl propargyl ether; 2-methylbenzofuran; masked salicylaldehyde; coumarin synthesis

Coumarins are widely distributed in nature[1] and have been reported to exhibit various biological and/or pharmacological activities.[1a,2] We have been studying the chemical constituents of Rutaceous plants containing coumarins, benzo[*c*]phenanthridine alkaloids, quinoline alkaloids, and others.[3] In 1982, Reisch *et al.* isolated a new coumarin having two methoxy groups and an (*E*)-3-oxo-1-butenyl side chain from *Toddalia asiatica* (Rutaceae) collected in India and proposed a formula (**1**) for its structure.[4] In this connection, we have reported the structural elucidation of an isomeric coumarin, toddalenone (**2**),[5] isolated from the same plant collected at Ishigaki island, Okinawa.[6] In the course of structural study on **2**, we synthesized 5-methoxysuberenon (**1**)[5] by chemical conversion from toddalolactone (**3**). However, since there were some discrepancies between the data for Reisch's coumarin and **1** as can be seen from Table I, we concluded that Reisch's new coumarin is neither 5-methoxysuberenon (**1**) nor toddalenone (**2**). So we have re-examined the structure of Reisch's coumarin on the basis of the reported spectral data.

It is generally known that simple 5-alkoxy and 5-alkylcoumarins show the C_4-H signal between δ 7.9 and δ 8.2 in the ^{1}H-nuclear magnetic resonance (NMR) spectra.[7] The ^{1}H-NMR spectrum of Reisch's coumarin showed the signal assignable to C_4-H at δ 8.00, allowing us to locate the (*E*)-3-oxo-1-butenyl side chain at the C_5-position. Furthermore, all of the coumarins isolated from Rutaceous plants bear an oxygen function at the C_7-position. Bases on these results, two formulas, 6,7-dimethoxy- and 7,8-dimethoxy-5-[(*E*)-3-oxo-1-butenyl]-coumarins (**4** and **5**), can be considered for Reisch's coumarin. Thus, we planned to synthesize the two coumarins (**4** and **5**) by taking advantage of our novel synthetic methods *i.e.* i) a salicylaldehyde synthesis *via* the cesium fluoride (CsF)-mediated Claisen rearrangement of an aryl propargyl ether and subsequent oxidative cleavage of the 2-methylbenzofuran and hydrolysis,[8] and ii) a coumarin synthesis by the Wittig reaction of the salicylaldehyde.[9] Moreover, we planned to investigate the utility of 2-methylbenzofurans as not only a source of C_1 unit at the *ortho* position of a phenolic group but also a protecting group for phenol.[8] The details of these results are the subject of this paper.

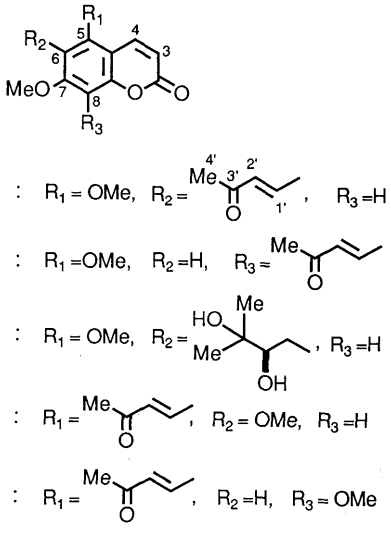

Chart 1

We designed the synthetic route for **4** shown in Chart 2, involving that the common intermediate (**14**), which could be prepared by the two routes starting from vanillin *i.e.* route A *via* isoscopoletin (**12**) and route B *via* benzofuran (**19**).[10] Recently, we succeeded in the synthesis of phenolic benzo[*c*]phenanthridine alkaloids by using an isopropyl group as a phenol-protecting group, which resists hydrogenolysis and can be removed with sulfuric acid in acetic acid.[11,12] Therefore, we chose an isopropyl group as a protecting group of the phenolic function of vanillin and first investigated route A. Thus, treatment of vanillin with isopropyl bromide and potassium carbonate in *N*,*N*-dimethylformamide (DMF) gave the isopropyl ether (**6**)[13] in 94.6% yield, and this was converted to the phenol (**7**) in 73.6% yield by Baeyer–Villiger (B.V.) oxidation with performic acid followed by alkaline hydrolysis. Reaction of **7** with benzyl chloride in the presence of potassium carbonate in DMF gave the benzyl ether (**8**) in 95.5% yield. This in turn was subjected to Vilsmeier–Haack reaction with DMF and phosphorus oxychloride to afford the aldehyde (**9**) in 96.6% yield. Hydrogenolysis of **9** with 5% palladium on carbon (Pd–C) under a hydrogen atmosphere provided the salicylaldehyde (**10**) in 92.7% yield.

Subsequently, the synthetic method[9a] for coumarin using Wittig reagent was applied to **10**. Thus, reaction of **10** with carbethoxymethylenetriphenylphosphorane in *N*,*N*-diethylaniline at 210 °C gave the desired coumarin (**11**) in an excellent yield.[14] Cleavage of the isopropoxy group of **11**

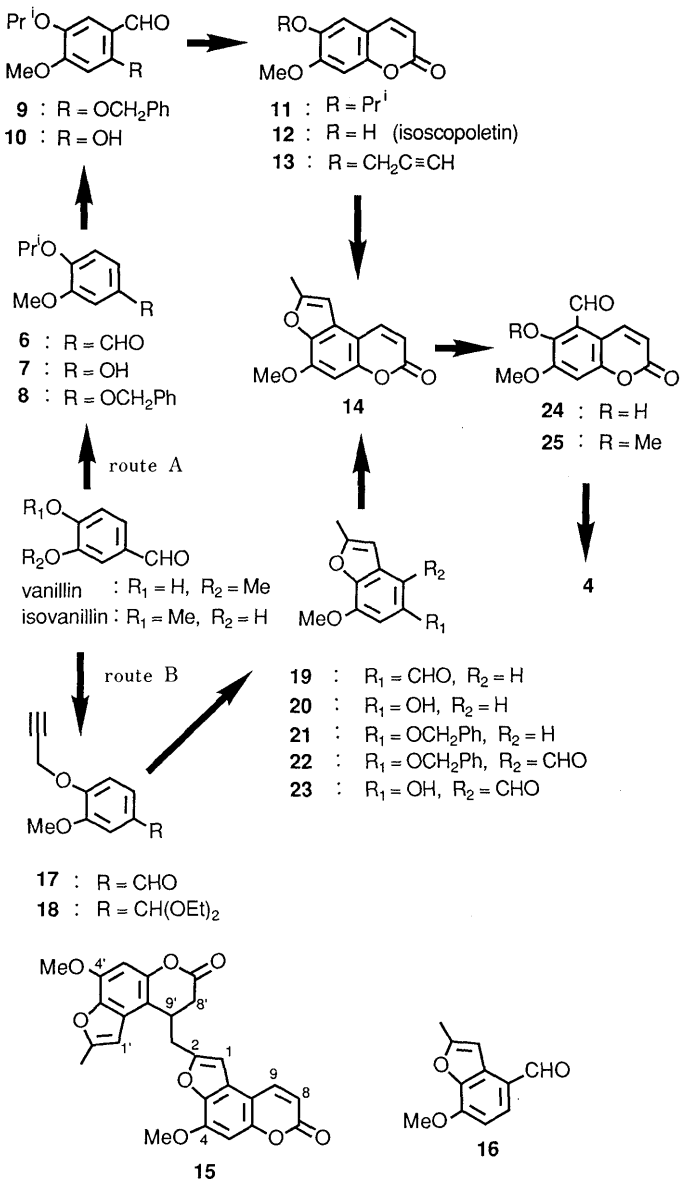

Chart 2

with a 5% solution (w/v) of concentrated sulfuric acid in acetic acid[11,12] gave isoscopoletin (6-hydroxy-7-methoxycoumarin) (**12**)[15] in 96.5% yield. Treatment of **12** with propargyl bromide provided the ether (**13**) in 96.8% yield, and this was subjected to the CsF-mediated Claisen rearrangement developed by us.[8] Thus, reaction of **13** in *N*,*N*-diethylaniline in the presence of CsF at 190—195 °C provided the common intermediate (**14**) in 57.6% yield along with a by-product (**15**). The structure of **15** was elucidated on the basis of the elemental analysis and spectral data. The molecular formula of **15** was in agreement with $C_{26}H_{20}O_8$ (*m*/*z* 460, M^+), indicating that **15** is a dimer of **13**. Absorption bands due to the δ-lactone and coumarin carbonyl groups were observed at 1760 and 1720 cm^{-1}, respectively, in its infrared (IR) spectrum. In spite of the presence of signals due to two methoxy groups, the signals due to only one methyl group and two sets of methylene groups were observed in its ^{1}H-NMR spectrum (see Experimental). Each signal was assigned on the basis of two-dimensional NMR [^{1}H–^{1}H and ^{1}H–^{13}C correlated spectra (COSY), and ^{1}H–^{13}C long range COSY (J=10, 5 Hz)] spectra. Observation of nuclear Overhauser effect (NOE) enhancement between $C_{1'}$-H (δ 6.41) and the methine proton (δ 3.73) in the NOE correlation spectroscopy and difference NOE experiments allowed us to deduce that the dimeric compound should be depicted as **15**, suggesting that a carbanion generated at C_2-Me on the bezofuran ring in **14** attacks at C_9 in a Michael addition manner to produce the dimer (**15**). The common intermediate (**14**) was, thus, prepared from vanillin in 30.4% overall yield *via* nine steps.

Next, synthesis of **14** through route B was studied. We recently reported the preparation of a benzofuran (**16**) from isovanillin in connection with synthetic studies on some natural products having four successive substituents on a benzene ring.[9b,16,17] The same procedures were used for the synthesis of **14** by route B. Thus, reaction of vanillin with propargyl bromide gave the propargyl ether (**17**) in 87.3% yield, and this was transformed to the acetal (**18**) in 79.9% yield by acetalization with ethyl orthoformate in ethanol. The CsF-mediated Claisen rearrangement of **18** followed by acid treatment gave the benzofuran-aldehyde (**19**) in 64.5% yield.[18] We have reported[9b] that B. V. oxidation of **16** with selenium dioxide and 30% hydrogen peroxide in methylene chloride[19] followed by alkaline hydrolysis gave the expected phenol in high yield. However, application of this procedure to **19** resulted in recovery of the starting material. Then, oxidation of **19** with an ordinary peracid was examined. Subsequent treatment of **19** with performic acid and alkaline hydrolysis afforded, in a moderate yield, a very labile phenol (**20**) which was immediately converted to benzyl ether (**21**) in 57.5% yield. Vismeier–Haack reaction of **21** with DMF and phosphorus oxychloride afforded the desired aldehyde (**22**) in 85.7% yield. The ^{1}H-NMR spectrum of **22** showed a signal attributed to an aromatic proton at δ 7.18 as a 1H singlet, allowing us to deduce that the formyl group was introduced at C_4, not at C_3. The structure of **22** was finally determined by transformation to **14** (*vide infra*). Hydrogenolysis of **22** on 5% Pd–C provided the salicylaldehyde (**23**) in 91.5% yield. This product was reacted with carbethoxymethylenetriphenylphosphorane in *N*,*N*-diethylaniline to give the common intermediate coumarin (**14**) mentioned above in 80.4% yield. In contrast to the yield *via* route A, the overall yield *via* route B was only 5.7% in eight steps.

In order to oxidize the benzofuran ring, the method using osmium tetroxide[8] was applied to **14**. However, since dihydroxylation was very sluggish, another method was studied. Thus, successive treatment of **14** with peracid prepared from trifluoroacetic anhydride and 30% hydrogen peroxide,[20] oxidative cleavage with sodium metaperiodate and alkaline hydrolysis afforded the salicylaldehyde (**24**)[21] in 44.2% yield, and this was methylated with dimethyl sulfate to afford the methyl ether (**25**) in 90.0% yield. Finally, aldol condensation of **25** with acetone gave one (**4**) of the candidates for Reisch's coumarin in 66.2% yield. These results strongly indicate that the furan ring in 2-methylbenzofuran can act effectively as not only a source of C_1 unit but also a protecting group for phenol.

Synthesis of the other candidate (**5**) for Reisch's coumarin was next studied. The synthetic strategy starting from 3,4,5-trimethoxytoluene is shown in Chart 3. Vilsmeier–Haack reaction of 3,4,5-trimethoxytoluene with DMF and

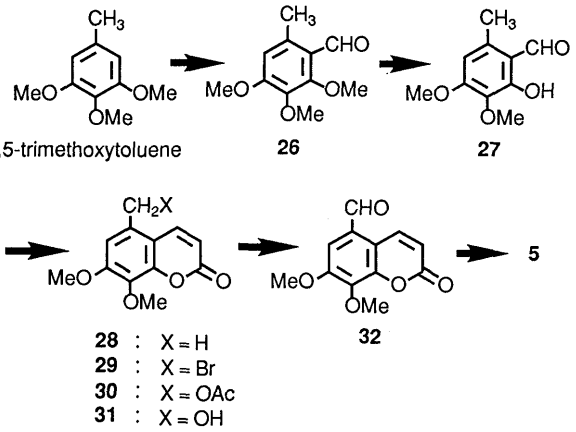

Chart 3

TABLE I. Melting Points and NMR Data[a] of the Coumarins

	Reisch's coumarin[b]	1	2	4	5
mp (°C)	176—180	199—200	244—246	184—185.5	215—216
^{1}H-NMR					
OMe	3.80 s	3.85 s	3.99 s	3.82 s	4.00 s
OMe	4.00 s	3.97 s	4.00 s	3.96 s	4.03 s
1′-H	7.50 d (17.0)	7.76 d (16.8)	7.94 d (16.5)	7.75 d (16.5)	7.89 d (15.7)
2′-H	6.60 d (17.0)	7.16 d (16.8)	7.25 d (16.5)	6.70 d (16.5)	6.72 d (15.7)
CMe	2.38 s	2.40 s	2.41 s	2.44 s	2.43 s
3-H	6.30 d (9.5)	6.29 d (9.6)	6.20 d (9.6)	6.31 d (9.9)	6.37 d (9.9)
4-H	8.00 d (9.5)	7.91 d (9.6)	7.99 d (9.6)	7.92 d (9.9)	8.00 d (9.9)
6- or 8-H	6.76 s	6.67 s	6.34 s	6.89 s	7.10 s
^{13}C-NMR					
OMe		56.12	56.39	56.27	56.44
OMe		56.20	63.19	60.93	61.62
$C_{1'}$		131.75	132.67	134.47	137.90
$C_{2'}$		129.89	131.12	134.78	129.97
$C_{3'}$		199.92	199.42	197.70	197.15
$C_{4'}$		27.56	27.65	28.09	28.32
C_3		111.38	113.33	113.89	114.39
C_4		138.52	138.40	140.24	139.01
C_6		90.21			106.43
C_8			96.00	101.40	
Others		103.81	107.62	110.25	112.90
		104.72	114.05	126.23	127.43
		154.97	156.91	144.88	137.90
		158.24	158.00	152.55	148.46
		160.32	160.27	155.88	155.04
		163.11	162.44	160.44	159.57

a) ^{1}H-(500 MHz) and ^{13}C-NMR (125 MHz) spectra were measured in $CDCl_3$ solution. Chemical shifts are given in δ (ppm) and the values in parentheses in ^{1}H-NMR data are coupling constants in Hz. ^{13}C-NMR assignments are based on H–C COSY. *b*) For this coumarin the data was those of the 60 MHz ^{1}H-NMR (in $CDCl_3$) spectrum. (See reference 4.)

phosphorus oxychloride gave the aldehyde (**26**)[22] in 82.7% yield. Selective demethylation of **26** with boron trichloride[23] in methylene chloride afforded the expected salicylaldehyde (**27**)[22] in 78.3% yield, whereas demethylation with aluminum trichloride[22] or boron tribromide[24] gave unsatisfactory results. Coumarin ring formation of **27** with the Wittig reagent proceeded smoothly to provide the coumarin (**28**) in 90.0% yield. Since direct oxidation of the methyl group in **28** to an aldehyde group with selenium dioxide,[25] benzeneseleninic anhydride,[26] ceric(IV) ammonium nitrate,[27] or 2,3-dichloro-5,6-dicyanobenzoquinone[28] was not fruitful, oxidation with *N*-bromosuccinimide (NBS) was then examined. Reaction of **28** with 1.1 eq of NBS in the presence of benzoyl peroxide in benzene[29] afforded the desired monobromide (**29**) in 53.4% yield.[30,31] The molecular formula of **29** was in agreement with $C_{12}H_{11}BrO_4$. Its structure was elucidated on the basis of the signals due to C_3-H at δ 6.39 (1H, d, J=9.9 Hz), C_4-H at δ 7.93 (1H, d, J=9.9 Hz), and the bromomethyl group at δ 4.63 (2H, s) in its ^{1}H-NMR spectrum. Reaction of **29** with sodium acetate in acetic acid gave **30** in 81.4%, which was hydrolyzed with alkali to give **31** in 66.0% yield. In order to improve the yield, direct substitution of bromine to a hydroxy group was attempted. Treatment of **29** with silver oxide in aqueous dioxane[32] provided the desired alcohol (**31**) in high yield.[33,34] Subsequently, **31** was oxidized with pyridinium chlorochromate (PCC) to afford the aldehyde (**32**) in 90.4% yield. Aldol condensation of **32** with acetone gave the other candidate (**5**) for Reisch's coumarin in a moderate yield.

Melting points and NMR spectral data of the synthesized coumarins (**4** and **5**), 5-methoxysuberenon (**1**),[5] toddalenone (**2**),[5] and Reisch's coumarin[4] are listed in Table I, and the data of **4** are the most similar to those reported for Reisch's coumarin. Unfortunately, direct comparison of our samples with the natural sample and/or its spectral data could not be made because of their non-availability.

Experimental

Melting points were measured on a micro melting point hot-stage apparatus (Yanagimoto) and are uncorrected. IR spectra were recorded in Nujol on a Hitachi 215 spectrometer, ultraviolet (UV) spectra in methanol on a Hitachi U-3400, and NMR spectra in deuterio-chloroform on Hitachi R-24B (60 MHz), JEOL FX-270 (270 MHz), JEOL GSX-400 (400 MHz) and/or GSX-500 (500 MHz) spectrometers, unless otherwise noted. The NMR data are reported in parts per million downfield from tetramethylsilane as an internal standard (δ 0.0) and coupling constants in hertz. Electron impact mass spectra (EIMS) were taken on a Hitachi M-60 spectrometer (direct inlet) at 70 eV. First atom bombardment high-resolution MS (FAB-HRMS) were taken on a JEOL JMS-MX 110A and for measurement, each sample was dissolved in a matrix of *m*-nitrobenzyl alcohol and the solution was bombarded with a beam of neutral Xe atoms at an energy of 3 keV. Column chromatography was carried out on aluminum oxide (Woelm, W200, neutral), silica gel (Merck, Silica gel 60, No. 7734) or silica gel (Nacalai Tesque, Inc., Silica gel 60, 230—400 mesh). In general, the extract was washed with brine, dried over anhydrous K_2CO_3, then filtered, and the filtrate was evaporated to dryness under reduced pressure, unless otherwise noted. CsF was heated and powdered under an argon atmosphere and NH_4Cl was sublimed at 200 °C (2 mmHg) before use. Compounds for which no melting point is given are oily.

4-Isopropoxy-3-methoxybenzaldehyde (6) A suspension of vanillin (50 g, 0.33 mol), isopropyl bromide (47 ml, 0.5 mol), and K_2CO_3 (73.4 g, 0.53 mol) in DMF (250 ml) was stirred at 60—65 °C for 6 h, poured into a large quantity of water, and extracted with ether. The ethereal extract was washed with 5% aqueous NaOH solution. The residue was distilled under reduced pressure to give **6** (60.4 g, 94.6%), bp 123—130 °C (4 mmHg) (lit.[13] 150—152 °C (13 mmHg)). IR (neat): 1685 (C=O) cm^{-1}. ^{1}H-NMR (60 MHz): 1.43 (6H, d, J=6.0 Hz, $CH\underline{Me}_2$), 3.91 (3H, s, OMe), 4.69 (1H, heptet, J=6.0 Hz, $OC\underline{H}Me_2$), 6.96 (1H, d, J=8.5 Hz, C_5-H), 7.40 (1H, d, J=2.0 Hz, C_2-H), 7.41 (1H, dd, J=8.5, 2.0 Hz, C_6-H), 9.82 (1H, s, CHO).

4-Isopropoxy-3-methoxyphenol (7) To 85% HCO_2H (88 ml) was added 30% H_2O_2 (130 ml, 0.29 mol) at 0—5 °C, and the solution was stirred at room temperature for 1 h. After dropwise addition of a solution of **6** (30 g, 0.155 mol) in 98% HCO_2H (27 ml) to the above peracid solution at 0—5 °C over 70 min, the reaction mixture was stirred at the same temperature for a further 3.5 h. The excess of peracid was decomposed with Na_2SO_3 (33.8 g, 0.26 mol), then the mixture was diluted with water, and extracted with ether. The extract was washed with water and concentrated to about 100 ml under reduced pressure. A 5% aqueous NaOH solution (60 ml) was added to the concentrated ethereal solution and the mixture was vigorously stirred at room temperature for 30 min. The aqueous solution was separated and the ethereal solution was washed with 5% aqueous NaOH solution. The combined alkaline solution was acidified with 10% aqueous HCl solution, and extracted with ether, then the extract was dried over $MgSO_4$. The

residue was distilled under reduced pressure to give **7** (20.74 g, 73.6%), bp 125—129 °C (2 mmHg), mp 38—44 °C. *Anal.* Calcd for $C_{10}H_{14}O_3$: C, 65.91; H, 7.74. Found: C, 65.69; H, 7.66. IR ($CHCl_3$): 3400 (OH) cm^{-1}. ^{1}H-NMR (60 MHz): 1.29 (6H, d, J=6.0 Hz, $CHMe_2$), 3.73 (3H, s, OMe), 4.32 (1H, heptet, J=6.0 Hz, $OCHMe_2$), 5.50 (1H, br s, OH, disappeared on adding D_2O), 6.28 (1H, dd, J=8.0, 3.0 Hz, C_6-H), 6.42 (1H, d, J=3.0 Hz, C_2-H), 6.76 (1H, d, J=8.0 Hz, C_5-H).

4-Benzyloxy-1-isopropoxy-2-methoxybenzene (8) A suspension of **7** (15.39 g, 84.4 mmol), benzyl chloride (14.6 ml, 127 mmol), and K_2CO_3 (18.44 g, 133 mmol) in DMF (34 ml) was stirred at 60—70 °C for 12.5 h. The mixture was diluted with water and extracted with ether. The extract was washed with 5% aqueous NaOH solution and brine. The residue was distilled under reduced pressure to give **8** (21.97 g, 95.5%), bp 147—152 °C (2 mmHg), mp 33—34 °C. *Anal.* Calcd for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 74.92; H, 7.43. ^{1}H-NMR (60 MHz): 1.31 (6H, d, J=6.0 Hz, $CHMe_2$), 3.79 (3H, s, OMe), 4.35 (1H, heptet, J=6.0 Hz, $OCHMe_2$), 4.99 (2H, s, OCH_2Ph), 6.42 (1H, dd, J=8.0, 3.0 Hz, C_5-H), 6.58 (1H, d, J=3.0 Hz, C_3-H), 6.82 (1H, d, J=8.0 Hz, C_6-H), 7.37 (5H, br s, aromatic protons).

2-Benzyloxy-5-isopropoxy-4-methoxybenzaldehyde (9) Phosphorus oxycholoride (11.7 ml, 126 mmol) was added dropwise to DMF (9.5 ml, 123 mmol) under water cooling and the mixture was stirred at room temperature for 15 min. A solution of **8** (22.10 g, 81.2 mmol) in CH_2Cl_2 (54 ml) was added to the above solution and stirred at room temperature for 6 h. The reaction mixture was made alkaline with 5% aqueous NaOH solution under ice-cooling and was extracted with ether. The extract was washed with 5% aqueous NaOH solution and brine, dried, and evaporated to dryness to give oily **9** (23.53 g, 96.6%). A small quantity of **9** was distilled for characterization to afford a pure sample of **9**, bp 180—185 °C (1 mmHg), mp 57—62 °C. *Anal.* Calcd for $C_{18}H_{20}O_4$: C, 71.98; H, 6.71. Found: C, 71.76; H, 6.70. IR: 1660 (C=O) cm^{-1}. ^{1}H-NMR (60 MHz): 1.33 (6H, d, J=6.0 Hz, $CHMe_2$), 3.87 (3H, s, OMe), 4.49 (1H, heptet, J=6.0 Hz, $OCHMe_2$), 5.16 (2H, s, OCH_2Ph), 6.53 (1H, s, C_3-H), 7.38 (6H, br s, C_6-H and aromatic protons), 10.31 (1H, s, CHO).

2-Hydroxy-5-isopropoxy-4-methoxybenzaldehyde (10) A mixture of **9** (45.94 g, 0.15 mol) and 5% Pd–C (2.3 g) in MeOH (1500 ml) was hydrogenated at room temperature under atmospheric pressure until absorption of hydrogen ceased. The catalyst was filtered off on a Celite bed and the filtrate was evaporated under reduced pressure. The residue was recrystallized from EtOH to afford **10** (29.80 g, 92.7%), mp 83.5—85.5 °C (pale yellow needles). *Anal.* Calcd for $C_{11}H_{14}O_4$: C, 62.84; H, 6.71. Found: C, 62.89; H, 6.71. IR: 1650 (C=O) cm^{-1}. ^{1}H-NMR (60 MHz): 1.33 (6H, d, J=6.0 Hz, $CHMe_2$), 3.89 (3H, s, OMe), 4.38 (1H, heptet, J=6.0 Hz, $OCHMe_2$), 6.44 (1H, s, C_3-H), 6.97 (1H, s, C_6-H), 9.65 (1H, s, CHO), 11.30 (1H, s, OH, disappeared on adding D_2O).

6-Isopropoxy-7-methoxycoumarin (11) A solution of **10** (299 mg, 1.42 mmol) and carbethoxymethylenetriphenylphosphorane (599 mg, 1.73 mmol) in *N*,*N*-diethylaniline (12 ml) was heated at 210—215 °C for 40 min under an argon atmosphere. After cooling, the reaction mixture was diluted with water and extracted with ether. The extract was thoroughly washed with 5% aqueous HCl solution and brine. The residue was subjected to chromatography on silica gel (Merck) with hexane–ether (2:1) to give **11** (317 mg, 95.2%), mp 126—128 °C (yellow prisms from hexane–CH_2Cl_2). *Anal.* Calcd for $C_{13}H_{14}O_4$: C, 66.65; H, 6.02. Found: C, 66.84; H, 6.08. IR: 1725 (C=O) cm^{-1}. ^{1}H-NMR (60 MHz): 1.37 (6H, d, J=7.0 Hz, $CHMe_2$), 3.91 (3H, s, OMe), 4.52 (1H, heptet, J=7.0 Hz, $OCHMe_2$), 6.24 (1H, d, J=10.0 Hz, C_3-H), 6.81 (1H, s, C_8-H), 6.93 (1H, s, C_5-H), 7.61 (1H, d, J=10.0 Hz, C_4-H).

Isoscopoletin (6-Hydroxy-7-methoxycoumarin) (12) A solution of **11** (7.005 g, 29.9 mmol) in AcOH (120 ml) containing concentrated H_2SO_4 (3.6 ml) was refluxed for 2.5 h. The mixture was poured into a large amount of water. The crystalline material was obtained by filtration and recrystallized from acetone to give **12** (5.546 g, 96.5%), mp 188—190 °C (yellow prisms). *Anal.* Calcd for $C_{10}H_8O_4$: C, 62.50; H, 4.20. Found: C, 62.59; H, 4.23. IR: 3560 (OH), 1730 (C=O) cm^{-1}. ^{1}H-NMR (270 MHz): 3.98 (3H, s, OMe), 5.60 (1H, s, OH), 6.29 (1H, d, J=9.6 Hz, C_3-H), 6.83 (1H, s, C_8-H), 6.97 (1H, s, C_5-H), 7.59 (1H, d, J=9.6 Hz, C_4-H).

7-Methoxy-6-(2-propynyloxy)coumarin (13) A suspension of **12** (5.457 g, 28.4 mmol) and K_2CO_3 (5.138 g, 37.2 mmol) in acetone (150 ml) was treated with propargyl bromide (4.397 g, 37.0 mmol). The mixture was refluxed for 7 h with stirring, poured into water, and then extracted with CH_2Cl_2. The residue was recrystallized from CH_2Cl_2 to give **13** (6.329 g, 96.8%), mp 190—191 °C (colorless needles). *Anal.* Calcd for $C_{13}H_{10}O_4$: C, 67.82; H, 4.38. Found: C, 67.68; H, 4.44. IR ($CHCl_3$): 3225 (≡C–H), 1730 (C=O) cm^{-1}. ^{1}H-NMR (270 MHz): 2.55 (1H, t, J=2.4 Hz, $CH_2C\equiv CH$), 3.95 (3H, s, OMe), 4.79 (2H, d, J=2.4 Hz, $OCH_2C\equiv CH$), 6.30 (1H, d, J=9.5 Hz, C_3-H), 6.86 (1H, s, C_8-H), 7.06 (1H, s, C_5-H), 7.63 (1H, d, J=9.5 Hz, C_4-H).

Claisen Rearrangement of Propargyl Ether (13): 4-Methoxy-2-methyl-7*H*-furo[3,2-*f*][1]-benzopyran-7-one (14) and 4-Methoxy-2-(8′,9′-dihydro-4′-methoxy-2′-methyl-7′*H*-furo[3,2-*f*][1′]-benzopyran-7′-oxo-9′-yl)methyl-7*H*-furo[3,2-*f*][1]-benzopyran-7-one (15) A suspension of **13** (1.10 g, 4.78 mmol) and CsF (3.62 g, 23.9 mmol) in *N*,*N*-diethylaniline (11 ml) was heated at 190—195 °C for 3 h under an argon atmosphere. The mixture was diluted with benzene. After removal of the insoluble material by filtration, the filtrate was washed with 2 N aqueous H_2SO_4 solution and brine. The residue in $CHCl_3$ was subjected to flash chromatography on silica gel (Nacalai Tesque). Elution with $CHCl_3$ gave **14** (634 mg, 57.6%), mp 178—179 °C (pale yellow needles from acetone). *Anal.* Calcd for $C_{13}H_{10}O_4$: C, 67.82; H, 4.38. Found: C, 67.77; H, 4.42. IR: 1725 (C=O), 1615 (C=C) cm^{-1}. ^{1}H-NMR (270 MHz): 2.54 (3H, d, J=0.9 Hz, C_2-Me), 4.05 (3H, s, OMe), 6.32 (1H, d, J=9.5 Hz, C_8-H), 6.60 (1H, br d, J=0.9 Hz, C_1-H), 6.72 (1H, s, C_5-H), 7.86 (1H, d, J=9.5 Hz, C_9-H). Successive elution with $CHCl_3$ gave **15** (75 mg, 13.8%), mp 299—301 °C (dec.) (pale yellow prisms from CH_2Cl_2–acetone). *Anal.* Calcd for $C_{26}H_{20}O_8$: C, 67.82; H, 4.38. Found: C, 67.44; H, 4.38. IR: 1760 (C=O), 1720 (C=O) cm^{-1}. ^{1}H-NMR (500 MHz in DMSO-d_6): 2.30 (3H, s, $C_{2'}$-Me), 2.82 (1H, br d, J=16.5 Hz, $C_{8'}$-Ha), 3.01—3.13 (3H, m, $C_{8'}$-Hb, C_2-H_2), 3.73 (1H, dd, J=14.0, 6.9 Hz, $C_{9'}$-H), 3.90 (3H, s, OMe), 4.03 (3H, s, OMe), 6.33 (1H, d, J=9.6 Hz, C_8-H), 6.41 (1H, s, $C_{1'}$-H), 6.62 (1H, s, $C_{5'}$-H), 6.97 (2H, s, C_1-H, C_5-H), 8.20 (1H, d, J=9.6 Hz, C_9-H). MS *m*/*z*: 460 (M^+).

3-Methoxy-4-(2-propynyloxy)benzaldehyde (17) To a mixture of vanillin (25.02 g, 166.4 mmol) and K_2CO_3 (29.50 g, 213.5 mmol) in DMF (65 ml) was added propargyl bromide (25.40 g, 213.5 mmol). The mixture was stirred at room temperature for 2 h and was diluted with water, and then extracted with ether. The extract was washed with 5% aqueous NaOH solution and brine. The residue was recrystallized from MeOH to afford **17** (27.29 g, 87.3%), mp 88—89 °C (colorless prisms). *Anal.* Calcd for $C_{11}H_{10}O_3$: C, 69.46; H, 5.30. Found: C, 69.34; H, 5.31. IR: 3250 (≡C-H), 2120 (C≡C), 1690 (C=O) cm^{-1}. ^{1}H-NMR (270 MHz): 2.57 (1H, t, J=2.6 Hz, $CH_2C\equiv CH$), 3.94 (3H, s, OMe), 4.86 (2H, d, J=2.6 Hz, $OCH_2C\equiv CH$), 7.14 (1H, d, J=8.1 Hz, C_5-H), 7.43 (1H, d, J=1.8 Hz, C_2-H), 7.46 (1H, dd, J=8.1, 1.8 Hz, C_6-H), 9.87 (1H, s, CHO).

3-Methoxy-4-(2-propynyloxy)benzaldehyde Diethyl Acetal (18) A mixture of **17** (500 g, 26.29 mmol), ethyl orthoformate (4.44 g, 29.97 mmol), and NH_4Cl (0.14 g, 2.70 mmol) in dry EtOH (5.1 ml) was heated under reflux for 3 h. The solvent and resulting ethyl formate were removed by distillation. The residue was dissolved in ether and the ethereal solution was washed with 5% aqueous $NaHCO_3$ solution. The residue was distilled under reduced pressure to give **18** (5.55 g, 79.9%), bp 138 °C (4 mmHg). *Anal.* Calcd for $C_{15}H_{20}O_4$: C, 68.20; H, 7.63. Found: C, 68.11; H, 7.52. IR: 3270 (≡C-H), 2120 (C≡C) cm^{-1}. ^{1}H-NMR (60 MHz): 1.23 (6H, t, J=7.0 Hz, 2×CH_2Me), 2.49 (1H, t, J=2.3 Hz, $CH_2C\equiv CH$), 3.59 (4H, q, J=7.0 Hz, 2×OCH_2Me), 3.87 (3H, s, OMe), 4.75 (2H, d, J=2.3 Hz, $OCH_2C\equiv CH$), 5.41 (1H, s, OCHO), 7.00 (3H, s, aromatic protons).

5-Formyl-7-methoxy-2-methylbenzo[*b*]furan (19) A suspension of **18** (21.70 g, 82.1 mmol) and CsF (21.52 g, 141.7 mmol) in *N*,*N*-diethylaniline (132 ml) was refluxed for 3 h under an argon atmosphere. The mixture was diluted with ether. After removal of the insoluble material by filtration, the filtrate was washed with 5% aqueous HCl solution and brine. The residue was subjected to chromatography on silica gel (Merck) with $CHCl_3$ to afford **19** (10.06 g, 64.5%), mp 105—106 °C (colorless prisms from hexane). *Anal.* Calcd for $C_{11}H_{10}O_3$: C, 69.46; H, 5.30. Found: C, 69.74; H, 5.35. IR: 1690 (C=O) cm^{-1}. ^{1}H-NMR (270 MHz): 2.50 (3H, d, J=0.3 Hz, C_2-Me), 4.05 (3H, s, OMe), 6.47 (1H, br d, J=0.3 Hz, C_3-H), 7.30 (1H, d, J=1.3 Hz, aromatic proton), 7.59 (1H, d, J=1.3 Hz, aromatic proton), 9.96 (1H, s, CHO).

5-Hydroxy-7-methoxy-2-methylbenzo[*b*]furan (20) To 85% HCO_2H (20 ml) was added 30% H_2O_2 (5.8 ml, 51.54 mmol) under ice-cooling, and the solution was stirred at room temperature for 30 min. After dropwise addition of a solution of **19** (5.026 g, 26.43 mmol) in 98% HCO_2H (35 ml) to the above solution at below 0 °C, the mixture was stirred at the same temperature for a further 5 h. The excess peracid was decomposed with Na_2SO_3 (6.1 g) and the reaction mixture was diluted with water, then extracted with ether. The extract was concentrated to about 50 ml under reduced pressure. To the concentrated ethereal solution was added 5% aqueous NaOH solution (50 ml), and the mixture was vigorously stirred at room temperature for 30 min. The aqueous solution was separated and the ethereal solution was further washed with 5% aqueous NaOH solution. The combined alkaline solution was acidified with 10% aqueous HCl

solution and then extracted with ether. The extract was dried over $MgSO_4$. The residue in CH_2Cl_2 was passed through a short column of silica gel (Merck) to give a crude phenol (**20**) (1.645 g, 35.0%). IR: 3400 (OH) cm^{-1}. ^{1}H-NMR (60 MHz): 2.40 (3H, s, C_2-Me), 3.90 (3H, s, OMe), 6.20 (1H, br s, C_3-H), 6.28 (1H, d, J=3.0 Hz, aromatic proton), 6.45 (1H, d, J=3.0 Hz, aromatic proton). This crude phenol was used for the next reaction without further purification.

5-Benzyloxy-7-methoxy-2-methylbenzo[*b*]furan (21) A suspension of **20** (1.645 g, 9.23 mmol), benzyl chloride (1.77 ml, 15.41 mmol), and K_2CO_3 (2.692 g, 19.48 mmol) in DMF (4 ml) was stirred at 60—70 °C for 5 h. The mixture was diluted with water and extracted with ether. The extract was washed with 1% aqueous NaOH solution. The residue was subjected to chromatography on silica gel (Merck) with hexane–AcOEt (9 : 1) to afford **21** (1.423 g, 57.5%), mp 64—65 °C (colorless prisms from benzene–hexane). *Anal.* Calcd for $C_{17}H_{16}O_3$: C, 76.10; H, 6.01. Found: C, 76.25; H, 6.09. ^{1}H-NMR (60 MHz): 2.45 (3H, s, C_2-Me), 3.95 (3H, s, OMe), 5.06 (2H, s, OCH_2Ph), 6.29 (1H, br s, C_3-H), 6.46 (1H, d, J=2.0 Hz, aromatic proton), 6.61 (1H, d, J=2.0 Hz, aromatic proton), 7.40 (5H, s, aromatic protons).

5-Benzyloxy-4-formyl-7-methoxy-2-methylbenzo[*b*]furan (22) Phosphorus oxychloride (0.62 ml, 6.63 mmol) was added to a solution of **21** (1.423 g, 5.30 mmol) in DMF (5.5 ml, 70.6 mmol) under ice-cooling and the mixture was stirred at 60—70 °C for 5 h. After cooling, the reaction mixture was diluted with saturated aqueous AcONa solution (33 ml) and extracted with ether. The extract was washed with 5% aqueous NaOH solution and brine. The residue was recrystallized from benzene to afford **22** (1.346 g, 85.7%), mp 138—139 °C (colorless prisms). *Anal.* Calcd for $C_{18}H_{16}O_4$: C, 72.96; H, 5.44. Found: C, 72.92; H, 5.47. IR: 1658 (C=O) cm^{-1}. ^{1}H-NMR (500 MHz): 2.47 (3H, s, C_2-Me), 4.03 (3H, s, OMe), 5.19 (2H, s, CH_2Ph), 6.39 (1H, s, C_3-H), 7.18 (1H, s, C_6-H), 7.40 (5H, s, aromatic protons), 10.51 (1H, s, CHO).

5-Hydroxy-4-formyl-7-methoxy-2-methylbenzo[*b*]furan (23) A mixture of **22** (3.142 g, 10.60 mmol) and 5% Pd–C (0.23 g) in AcOEt (102 ml) was hydrogenated at room temperature under atmospheric pressure until absorption of hydrogen ceased. The catalyst was filtered off on a Celite bed and the filtrate was evaporated under reduced pressure. The residue was recrystallized from EtOH to give **23** (2.000 g, 91.5%), mp 146—147 °C (colorless needles). *Anal.* Calcd for $C_{11}H_{10}O_4$: C, 64.07: H, 4.89. Found: C, 63.79; H, 4.90. IR: 1630 cm^{-1}. ^{1}H-NMR (500 MHz): 2.49 (3H, s, C_2-Me), 4.03 (3H, s, OMe), 6.39 (1H, s, C_3-H), 6.63 (1H, s, C_6-H), 10.03 (1H, s, CHO), 11.92 (1H, s, OH).

Reaction of 23 with Wittig Reagent: Compound 14 A solution of **23** (2.049, 9.94 mmol) and carbethoxymethylenetriphenylphosphorane (3.936 g, 14.51 mmol) in *N*,*N*-diethylaniline (40 ml) was heated at 210—215 °C for 30 min under an argon atmosphere. After cooling, the reaction mixture was diluted with water and extracted with a large quantity of ether. The extract was thoroughly washed with 5% aqueous HCl solution and brine. The residue was subjected to chromatography on silica gel (Merck) with benzene–AcOEt (6 : 1) to give **14** (1.839 g, 80.4%), mp 176—179 °C (pale yellow needles from acetone). This compound was identical with the sample (**14**) prepared above.

5-Formyl-6-hydroxy-7-methoxycoumarin (24) To trifluoroacetic anhydride (12.0 ml, 85.1 mmol) was added dropwise 30% H_2O_2 (1.61 ml, 15.8 mmol) under ice-cooling. The above solution containing peracid was directly added to **14** (0.732 g, 3.18 mmol) at −4—−2 °C with stirring. The mixture was stirred below 0 °C for 30 min and poured into ice-water. The excess of peracid was decomposed with $NaHSO_3$, basified with saturated aqueous $NaHCO_3$ solution, and then extracted with AcOEt. A small amount of the residue was purified by recrystallization for characterization to give colorless prisms, mp 202—206.5 °C (from acetone–hexane). *Anal.* Calcd for $C_{13}H_{12}O_6$: C, 59.09; H, 4.58. Found: C, 59.03; H, 4.57. $NaIO_4$ (1.307 g, 6.11 mmol) was added to a solution of the crude product (0.730 g) in MeOH (137 ml) and water (42 ml). The mixture was stirred at room temperature for 1 h, poured into water, and then extracted with $CHCl_3$. A suspension of the crude product (0.695 g) in EtOH (84.2 ml) and 1% aqueous $NaHCO_3$ solution (63.7 ml) was refluxed for 1.5 h. After cooling, the mixture was poured into water, acidified with 5% aqueous HCl solution and then extracted with $CHCl_3$. The extract was dried over $MgSO_4$. The residue was recrystallized from $CHCl_3$–MeOH to give **24** (0.309 g, 44.2%), mp 255—259 °C (softened at 240 °C) (pale yellow prisms) (lit.[21] mp 245—246 °C). *Anal.* Calcd for $C_{11}H_8O_5$: C, 60.00; H, 3.66. Found: C, 59.77; H, 3.67. IR: 3150 (OH), 1770 (C=O), 1665 (C=O) cm^{-1}. ^{1}H-NMR (60 MHz): 4.05 (3H, s, OMe), 6.46 (1H, d, J=9.5 Hz, C_3-H), 7.10 (1H, s, C_8-H), 8.67 (1H, d, J=9.5 Hz, C_4-H), 10.65 (1H, s, CHO).

5-Formyl-6,7-dimethoxycoumarin (25) A mixture of **24** (139 mg, 6.2 mmol), benzyltributylammonium chloride (62 mg, 1.9 mmol), Me_2SO_4 (390 mg, 30.9 mmol), and 10% aqueous NaOH solution in CH_2Cl_2 (6.8 ml) was stirred at room temperature for 2 h. The mixture was diluted with water and extracted with CH_2Cl_2. The extract was washed with 5% aqueous NH_4OH solution and brine. The residue was recrystallized from AcOEt to provide **25** (129 mg, 90.0%), mp 195—206 °C (sublimation) (pale yellow fine needles). *Anal.* Calcd for $C_{12}H_{10}O_5$: C, 61.54; H, 4.30. Found: C, 61.38: H, 4.34. IR: 1732 (C=O), 1717 (C=O), 1686 (C=O) cm^{-1}. ^{1}H-NMR (60 MHz): 4.05 (6H, s, 2 × OMe), 6.40 (1H, d, J=9.5 Hz, C_3-H), 7.08 (1H, s, C_8-H), 8.91 (1H, d, J=9.5 Hz, C_4-H), 10.55 (1H, s, CHO).

6,7-Dimethoxy-5-[(*E*)-3-oxo-1-butenyl]coumarin (4) A 2% aqueous NaOH solution (0.35 ml) was added to a solution of **25** (24.6 mg, 1.05 mmol) in acetone (1.1 ml), and the reaction mixture was stirred at room temperature for 1 d. The mixture was diluted with water and extracted with AcOEt. The residue was recrystallized from acetone to afford **4** (13.5 mg, 66.2%), mp 186.5—188.5 °C (pale yellow fine needles). *Anal.* Calcd for $C_{15}H_{14}O_5$: C, 65.69; H, 5.15. Found: C, 65.59; H, 5.20. FAB-HRMS *m*/*z*: Calcd for $C_{15}H_{15}O_5$ (MH^+): 275.0919. Found: 275.0920. IR: 1740 (C=O), 1710 (C=O), 1660 (C=C) cm^{-1}. UV λ_{max} (log ε): 203 (4.44), 228 (4.28), 274 (4.10) sh, 311 (4.14), 354 (3.96). ^{1}H- and ^{13}C-NMR data are given in Table I.

2,3,4-Trimethoxy-6-methylbenzaldehyde (26) Phosphorus oxychloride (4.2 ml, 45.0 mmol) was added to a solution of 3,4,5-trimethoxytoluene (2.999 g, 16.5 mmol) in DMF (5.0 ml, 64.9 mmol) below 10 °C. After stirring at 90 °C for 1 h, the mixture was diluted with saturated aqueous AcONa solution (30 ml) and extracted with ether. The extract was washed with 5% aqueous NaOH solution and brine. The residue was chromatographed on aluminum oxide with benzene to afford **26** (2.862 g, 82.7%), mp 57.5—59.5 °C (lit.[22] mp 60—61 °C) (pale yellow plates). *Anal.* Calcd for $C_{11}H_{14}O_4$: C, 62.85; H, 6.71. Found: C, 62.91; H, 6.75. IR: 1680 (C=O) cm^{-1}. ^{1}H-NMR (60 MHz): 2.58 (3H, s, Me), 3.88 (3H, s, OMe), 3.94 (3H, s, OMe), 4.00 (3H, s, OMe), 6.53 (1H, s, C_5-H), 10.37 (1H, s, CHO).

2-Hydroxy-3,4-dimethoxy-6-methylsalicylaldehyde (27) Boron trichloride (6.1 ml, 71.0 mmol) was added to a solution of **26** (5.000 g, 23.8 mmol) in absolute CH_2Cl_2 (240 ml) at −78 °C and was stirred at the same temperature for 2.5 h. The mixture was carefully poured into ice-water with stirring and extracted with CH_2Cl_2. The organic layer was washed with 5% aqueous NaOH solution. The alkaline layer was acidified with 10% aqueous HCl solution and extracted with ether. The residue was recrystallized from ether to give **27** (3.655 g, 78.3%), mp 102—103 °C (lit.[22] mp 95—98 °C) (pale yellow plates). *Anal.* Calcd for $C_{10}H_{12}O_4$: C, 61.21; H, 6.17. Found; C, 61.15; H, 6.14. IR: 1640 (C=O) cm^{-1}. ^{1}H-NMR (60 MHz): 2.53 (3H, s, Me), 3.84 (3H, s, OMe), 3.91 (3H, s, OMe), 6.30 (1H, s, C_5-H), 10.09 (1H, s, CHO), 12.12 (1H, s, OH).

7,8-Dimethoxy-5-methylcoumarin (28) A solution of **27** (2.002 g, 10.20 mmol) and carbethoxymethylenetriphenylphosphorane (4.264 g, 12.24 mmol) in *N*,*N*-diethylaniline was heated at 210—215 °C for 30 min under an argon atomosphere. After cooling, the reaction mixture was diluted with a large quantity of ether. The ethereal solution was thoroughly washed with 5% aqueous HCl solution and brine. The residue was chromatographed on silica gel (Merck) with benzene–AcOEt (19 : 1) to afford **28** (2.033 g, 90.0%), mp 117.5—119.5 °C (colorless needles from hexane–CH_2Cl_2). *Anal.* Calcd for $C_{12}H_{12}O_4$: C, 65.44; H, 5.49. Found: C, 65.41; H, 5.54. IR: 1733 (C=O), 1711 (C=O) cm^{-1}. ^{1}H-NMR (500 MHz): 2.48 (3H, s, Me), 3.94 (3H, s, OMe), 3.95 (3H, s, OMe), 6.26 (1H, d, J=9.8 Hz, C_3-H), 6.70 (1H, s, C_6-H), 7.81 (1H, d, J=9.8 Hz, C_4-H).

5-Bromomethyl-7,8-dimethoxycoumarin (29) A solution of **28** (1.000 g, 4.54 mmol), NBS (0.890 g, 5.0 mmol), and benzoyl peroxide (0.021 g, 0.07 mmol) in benzene (10 ml) was refluxed for 20 min, then allowed to cool. Insoluble material was filtered off and the filtrate was evaporated under reduced pressure. The residue was recrystallized from $CHCl_3$–ether to give **29** (0.726 g, 53.4%), mp 159—160 °C (colorless needles). *Anal.* Calcd for $C_{12}H_{11}BrO_4$: C, 48.18; H, 3.71. Found: C, 48.10; H, 3.71. IR: 1730 (C=O) cm^{-1}. ^{1}H-NMR (500 MHz): 3.97 (3H, s, OMe), 4.00 (3H, s, OMe), 4.63 (2H, s, CH_2Br), 6.39 (1H, d, J=9.9 Hz, C_3-H), 6.88 (1H, s, C_6-H), 7.93 (1H, d, J=9.9 Hz, C_4-H).

5-Acetoxymethyl-7,8-dimethoxycoumarin (30) A solution of **29** (300 mg , 1.0 mmol) and fused AcONa (154 mg, 1.88 mmol) in AcOH (2 ml) was refluxed for 1 h. The reaction mixture was concentrated to dryness under reduced pressure and was subjected to chromatography on silica gel (Merck) with benzene–AcOEt (4 : 1) to give **30** (226 mg, 81.4%), mp 121—123 °C (colorless prisms from $CHCl_3$–ether). *Anal.* Calcd for $C_{14}H_{14}O_6$: C, 60.43; H, 5.07. Found: C, 60.13; H, 4.84. IR: 1740 (C=O) cm^{-1}. ^{1}H-NMR (60 MHz): 2.20 (3H, s, COMe), 4.00 (6H, s, 2 × OMe), 5.28 (2H, s, CH_2OAc), 6.33 (1H, d, J=10.0 Hz, C_3-H), 6.96

(1H, s, C_6-H), 7.90 (1H, d, J=10.0 Hz, C_4-H).

5-Hydroxymethyl-7,8-dimethoxycoumarin (31) i) Hydrolysis of **30**: A 2% aqueous NaOH solution (1.2 ml) was added to a solution of **30** (100 mg, 0.36 mmol) in MeOH (5 ml). The mixture was stirred at room temperature for 10 min, diluted with water, and then extracted with CH_2Cl_2. The residue was recrystallized from MeOH to give **31** (56 mg, 66.0%), mp 183—185 °C (colorless prisms). *Anal.* Calcd for $C_{12}H_{12}O_5$: C, 61.01; H, 5.12. Found: C, 61.04; H, 5.16. IR: 3400 (OH), 1690 (C=O) cm^{-1}. ^{1}H-NMR (500 MHz): 1.89 (1H, t, J=5.8 Hz, CH_2OH), 3.96 (3H, s, OMe), 3.98 (3H, s, OMe), 4.88 (2H, d, J=5.8 Hz, CH_2OH), 6.30 (1H, d, J=9.9 Hz, C_3-H), 6.93 (1H, s, C_6-H), 7.97 (1H, d, J=9.9 Hz, C_4-H).

ii) Reaction of **29** with Ag_2O: A mixture of **29** (500 mg, 1.67 mmol) and Ag_2O (638 mg, 2.76 mmol) in dioxane (27.5 ml) and water (3.5 ml) was stirred at room temperature for 2 h in the dark. The precipitate was filtered off and the filtrate was diluted with water, then extracted with $CHCl_3$. The extract was dried over $MgSO_4$. The residue was recrystallized from methanol to provide **31** (342 mg, 86.6%), mp 183—185 °C.

5-Formyl-7,8-dimethoxycoumarin (32) A mixture of **31** (152 mg, 0.64 mmol), pyridinium chlorochromate (276 mg, 1.28 mmol), and molecular sieves 3A (320 mg) in dry CH_2Cl_2 (2 ml) was stirred at room temperature for 10 min. The reaction mixture was diluted with CH_2Cl_2 and filtered through a Silica gel G (containing 13% $CaSO_4$) bed. The filtrate was evaporated under reduced pressure. The residue was recrystallized from CH_2Cl_2–ether to afford **32** (135 mg, 90.4%), mp 203—204 °C (colorless needles). *Anal.* Calcd for $C_{12}H_{10}O_5$: C, 61.54; H, 4.30. Found: C, 61.52; H, 4.40. IR: 1744 (C=O), 1712 (C=O), 1690 (C=C) cm^{-1}. ^{1}H-NMR (60 MHz): 4.03 (3H, s, OMe), 4.10 (3H, s, OMe), 6.43 (1H, d, J=10.0 Hz, C_3-H), 7.34 (1H, s, C_6-H), 8.91 (1H, d, J=10.0 Hz, C_4-H), 10.10 (1H, s, CHO).

7,8-Dimethoxy-5-[(*E*)-3-oxo-1-butenyl]coumarin (5) A 2% aqueous NaOH solution (3 ml) was added to a solution of **32** (250 mg, 1.48 mmol) in acetone (11 ml), and the mixture was refluxed for 1 d under an argon atmosphere. After cooling, the reaction mixture was diluted with water and extracted with AcOEt. The residue was chromatographed on silica gel (Merck) with benzene to give **5** (113 mg, 38.5%), mp 215—216 °C (colorless needles from acetone). *Anal.* Calcd for $C_{15}H_{14}O_5$: C, 65.69; H, 5.15. Found: C, 65.55; H, 5.16. FAB-HRMS *m/z*: Calcd for $C_{15}H_{15}O_5$ (MH^+): 275.0919. Found: 275.0922. IR: 1740 (C=O), 1710 (C=O), 1660 (C=C) cm^{-1}. UV λ_{max} (log ε): 202 (4.39), 224 (4.11) sh, 245 (4.03), 300 (4.14), 331 (4.21). IR: 1724 (C=O), 1668 (C=O) cm^{-1}. ^{1}H- and ^{13}C-NMR data are given in Table I.

Acknowledgements The authors thank the Ministry of Education, Science and Culture [Grant-in-Aid for Scientific Research (No. 01571141)] and Hoansha for financial support of this work.

References and Notes

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