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Total Synthesis of Coumarinolignans, Aquillochin (Cleomiscosin C) and Cleomiscosin D

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The reaction of 8-hydroxy-6-methoxy-7-methoxymethoxycoumarin (**3**) with ethyl 2-bromo-3-(4-benzyloxy-3,5-dimethoxyphenyl)-3-oxopropionate (**5**) in the presence of potassium *tert*-butoxide gave the condensation product (**6**), which, on treatment with hydrochloric acid followed by reduction with lithium borohydride, was converted into a diastereomeric mixture of alcohols (**8a**, **b**). Treatment of the alcohols (**8a**, **b**) with 35% hydrochloric acid in acetic acid furnished aquillochin (cleomiscosin C) (**1**). The regioisomer cleomiscosin D (**2**) was similarly synthesized from **10**.

Keywords——coumarinolignoid; aquillochin; cleomiscosin C; cleomiscosin D; fraxetin; coumarin; benzodioxane

Aquillochin (cleomiscosin C) (**1**) and the regioisomer cleomiscosin D (**2**) are members of a new class (coumarinolignoids)[1,2] of natural products. Aquillochin (**1**) has been isolated as a racemic form (no optical activity) from the stem wood of *Aquilaria agallocha* (Thymelaeaceae),[3] and also from seeds of *Cleome viscosa* (Capparidaceae)[4,5] along with the regioisomer cleomiscosin D, having no optical activity (racemic compound).

The synthesis of aquillochin (**1**) has been accomplished[6] by treatment of fraxetin and sinapyl alcohol under oxidative conditions (silver oxide and horseradish peroxidase) in low yield and accompanied with the formation of cleomiscosin D (**2**).

Herein, we describe a facile synthesis of **1** and **2** from readily available materials [8-hydroxy-6-methoxy-7-methoxymethoxycoumarin (**3**) or 8-benzyloxy-7-hydroxy-6-methoxycoumarin (**9**) and ethyl 3-(4-benzyloxy-3,5-dimethoxyphenyl)-2-bromo-3-oxopropionate (**5**)].

The compound (**3**)[2a] was condensed with **5** [prepared easily from ethyl 3-(4-benzyloxy-3,5-dimethoxyphenyl)-3-oxopropionate (**4**)[7] by bromination] in acetonitrile in the presence of potassium *tert*-butoxide to give a condensation product (**6**) in 67% yield. On treatment with hydrochloric acid at room temperature, the condensation product (**6**) was converted into a phenolic compound (**7**), which was then reduced with lithium borohydride in tetrahydrofuran (THF) at 0 °C to provide a mixture of alcohols (**8a**, **b**). The mixture (**8a**, **b**) was separated by high-performance liquid chromatography (HPLC) as described in the experimental section. Separation by HPLC provided **8a** as a main product and **8b** as a minor product. The high-resolution mass spectrum (MS) of each alcohol (**8a**, **b**) afforded the same molecular formula $C_{28}H_{28}O_{10}$ and the infrared (IR) spectra of **8a** and **8b** showed disappearance of the keto group band (1685 cm^{-1}) and the ester group band (1735 cm^{-1}) found in the starting material. In the proton nuclear magnetic resonance (^{1}H-NMR) spectrum of **8a**, the signal of the methine proton at the C-7′ position was observed as a doublet at δ 5.39 whose coupling constant was 2.7 Hz. On the other hand, the coupling constant of a doublet signal assigned to the C-7′ position (δ 5.23) in **8b** was 8.4 Hz. Therefore, [8] the signal observed at δ 5.39 was ascribed to the *erythro* isomer (**8a**) and **8b** was concluded to be the *threo* isomer. The ratio of the *erythro*

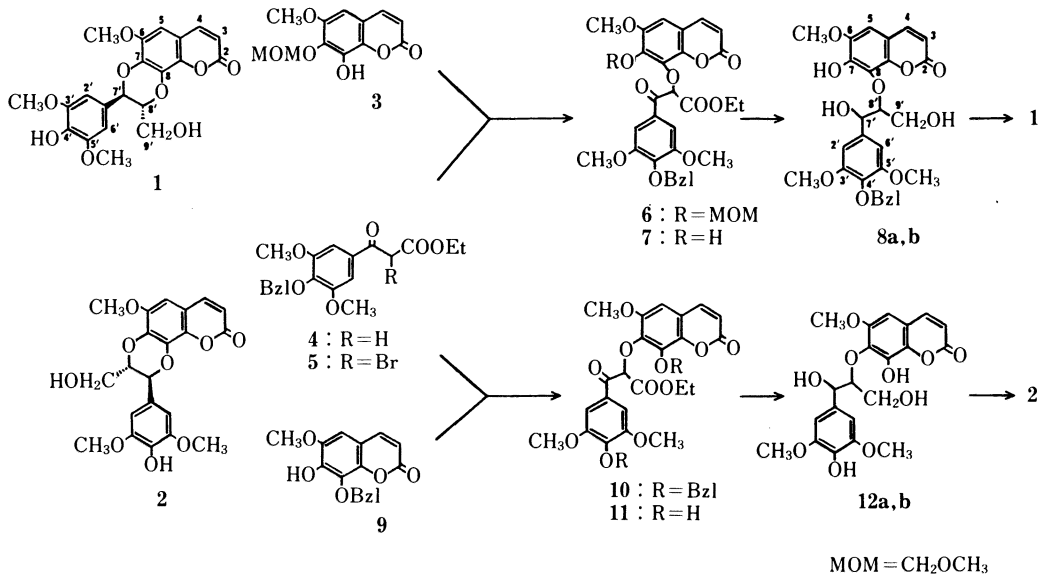

Chart 1

and *threo* isomer was about 2.5 : 1 on the basis of the peak areas in HPLC. The mixture of alcohols (**8a, b**) cyclized upon heating in acetic acid in the presence of 35% hydrochloric acid to give aquillochin (**1**), whose MS displayed the characteristic retro Diels–Alder fragmentation peak[4] at *m/z* 210. In the ^{1}H-NMR spectrum, the proton signal was observed as a doublet at δ 4.97 whose coupling constant was 8.1 Hz, demonstrating that two hydrogens of the benzodioxane moiety are *trans*-oriented. The synthetic aquillochin (**1**) was identical with an authentic specimen[4] based on comparisons of MS, IR (KBr), ^{1}H-NMR, and carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectra.

We also aimed at the synthesis of the regioisomer cleomiscosin D (**2**) according to the method described above. The starting material (8-benzylfraxetin) (**9**), prepared[2d] previously from **3**, was treated with **5** in the presence of potassium *tert*-butoxide to provide a condensation product (**10**) in 81% yield. The condensation product (**10**) was subjected to catalytic hydrogenation, affording a debenzylation product (**11**) in good yield. Reduction of **11** with lithium borohydride in THF at 0 °C gave a mixture of alcohols (**12a, b**), which was separated by chromatography on silica gel to yield the more-polar substance (**12a**, 45%) and the less-polar substance (**12b**, 4%). In the ^{1}H-NMR spectrum of **12a**, the methine proton at the C-7′ position was observed as a doublet at δ 5.20 (J = 3.7 Hz) and the methine proton in **12b** appeared as a doublet at δ 5.06 (J = 7.7 Hz). Hence, the alcohol (**12a**) was shown to be the *erythro* isomer and **12b** was the *threo* isomer. The ratio of the *erythro* and *threo* isomers was about 11 : 1 from the ^{1}H-NMR spectral analysis of the mixture (**12a, b**).

Finally, **12a, b** was treated with 35% hydrochloric acid in acetic acid to furnish cleomiscosin D (**2**). The ^{1}H-NMR spectrum and MS of **2** were closely similar to those of aquillochin (**1**). In the MS, the characteristic retro Diels–Alder fragmentation peak[5] appeared at *m/z* 210 and, in the ^{1}H-NMR spectrum, the C-7′ proton signal was observed as a doublet at δ 4.96 whose coupling constant (J = 8.1 Hz) was typical for *trans*-orientation of the benzodioxane moiety. The synthetic cleomiscosin D (**2**) was identical with an authentic sample[5] by direct comparison.

Thus, we have achieved the synthesis of aquillochin (cleomiscosin C) (**1**) and cleomiscosin D (**2**).

Experimental

All melting points are uncorrected. Column chromatography was run on Merck Silica gel 60 (70—230 mesh). Thin layer chromatography (TLC) was performed on glass plates precoated with Kieselgel 60 F_{254} (Merck). Electron impact (EI)-MS were recorded on a Hitachi M-52 spectrometer and high-resolution MS on a Hitachi M-80 spectrometer. Fast atom bombardment (FAB)-MS were recorded on JEOL JMS-DX300 and JEOL JMA-DA5000 spectrometer. IR spectra were obtained on a JASCO IR-810 spectrophotometer. ^{1}H-NMR spectra were recorded on a JEOL JNM-GX-270 and ^{13}C-NMR spectra on a JEOL JNM-FX-100 spectrometer with tetramethylsilane as an internal standard. Chemical shifts are quoted in parts per million (s=singlet, d=doublet, t=triple, q=quartet, m=multiplet, br=broad). HPLC was conducted on a JASCO TRI ROTAR-II instrument.

Ethyl 3-(4-Benzyloxy-3,5-dimethoxyphenyl)-2-bromo-3-oxopropionate (5)——A solution of *N*-bromosuccinimide (2.29 g) in $CHCl_3$ (30 ml) was added dropwise to a stirred solution of **4**[7] (4.6 g) in $CHCl_3$ (120 ml). Stirring was continued for 30 min, then the reaction mixture was washed three times with water, dried over Na_2SO_4, and evaporated. The crude product was chromatographed on a silica gel column (benzene–AcOEt (10 : 1)) to give a yellow oil (**5**, 950 mg, 54% based on consumed starting material) and the unaltered starting material (**4**, 3.17 g). High-resolution MS *m/z*: 438.0501 Calcd for $C_{20}H_{21}{}^{81}BrO_6$ ($M^+ + 2$). Found: 438.0511. High-resolution MS *m/z*: 436.0521 Calcd for $C_{20}H_{21}{}^{79}BrO_6$ (M^+). Found: 436.0496. MS *m/z*: 438 ($M^+ + 2$), 436 (M^+), 357, 347, 345, 311, 271. IR ($CHCl_3$): 3020, 1760, 1680, 1590 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.25 (3H, t, J=7.1 Hz, $OCH_2C\underline{H}_3$), 3.88 (6H, s, 2 × OCH_3), 4.28 (2H, q, J=7.1 Hz, $OC\underline{H}_2CH_3$), 5.13 (2H, s, $OC\underline{H}_2Ph$), 5.60 (1H, s, HCBr), 7.24 (2H, s, C_2-H and C_6-H), 7.27—7.48 (5H, m, aromatic protons).

Condensation of 3 with 5 (Formation of 6)——A solution of **5** (110 mg) in acetonitrile (2.0 ml) was added dropwise to a mixture of **3**[2a] (63 mg) and *tert*-BuOK (42 mg) in acetonitrile (4.0 ml). The mixture was stirred at room temperature for 10 min, poured into ice-water, and extracted with AcOEt. The AcOEt layer was washed with water, dried over Na_2SO_4, and evaporated. The residue was purified by preparative TLC ($CHCl_3$–acetone (20 : 1)) to give a colorless oil (**6**, 102 mg, 67%). FAB-MS *m/z*: 609 ($C_{32}H_{32}O_{12}+H)^+$. IR ($CHCl_3$): 1735, 1685, 1615, 1585 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.18 (3H, t, J=7.1 Hz, $OCH_2C\underline{H}_3$), 3.50 (3H, s, $OCH_2OC\underline{H}_3$), 3.87 (3H, s, OCH_3), 3.90 (6H, s, 2 × OCH_3), 4.24 (2H, q, J=7.1 Hz, $OC\underline{H}_2CH_3$), 5.13 (2H, s, $OC\underline{H}_2Ph$), 5.20 (1H, d, J=5.7 Hz, $OC\underline{H}_2OCH_3$), 5.23 (1H, d, J=5.7 Hz, $OC\underline{H}_2OCH_3$), 6.14 (1H, s, $C_{8'}$-H), 6.29 (1H, d, J=9.4 Hz, C_3-H), 6.70 (1H. s, C_5-H), 7.46 (2H, s, $C_{2'}$-H and $C_{6'}$-H), 7.27—7.49 (5H, m, aromatic protons), 7.58 (1H, d, J=9.4 Hz, C_4-H).

Hydrolysis of 6 (Formation of 7)——Saturated HCl–MeOH (2.0 ml) was added to a solution of **6** (105 mg) in MeOH (3.0 ml) and the resulting solution was stirred at room temperature for 5 min. The solvent was removed and the residue was dissolved with AcOEt. The AcOEt solution was washed with water, dried over Na_2SO_4, and evaporated. The crude product was purified by preparative TLC ($CHCl_3$–acetone (10 : 1)) to give a colorless oil (**7**, 93 mg, 95%). FAB-MS *m/z*: 565 ($C_{30}H_{28}O_{11}+H)^+$. IR ($CHCl_3$): 3630, 1735, 1685, 1585 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.23 (3H, t, J=7.1 Hz, $OCH_2C\underline{H}_3$), 3.90 (9H, s, 3 × OCH_3), 4.28 (1H, dq, J=7.1, 17.1 Hz, $OC\underline{H}_2CH_3$), 4.31 (1H, dq, J=7.1, 17.1 Hz, $OC\underline{H}_2CH_3$), 5.13 (2H, s, $OC\underline{H}_2Ph$), 6.15 (1H, s, $C_{8'}$-H), 6.25 (1H, d, J=9.4 Hz, C_3-H), 6.71 (1H, s, C_5-H), 7.27—7.48 (5H, m, aromatic protons), 7.45 (2H, s, $C_{2'}$-H and $C_{6'}$-H), 7.59 (1H, d, J=9.4 Hz, C_4-H), 8.35 (1H, br s, OH).

Reduction of 7 with Lithium Borohydride (Formation of 8a, b)——$LiBH_4$ (35 mg) was added gradually to a solution of **7** (156 mg) in dry THF (4.0 ml) at 0 °C and the resulting mixture was stirred at the same temperature for 15 min. The reaction mixture was poured into ice-water and extracted with AcOEt. The AcOEt layer was washed with water, dried over Na_2SO_4, and evaporated. The residue was purified by preparative TLC (benzene–AcOEt (1 : 1)) to give an oil (85 mg, 59%). A part of the oil (1.9 mg) was separated into **8a** (1.0 mg) and **8b** (0.3 mg) by HPLC. [conditions: column, YMC-Pack A-302 (ODS), 4.6 mm × 15 cm; flow rate, 1.5 ml/min; detector, UV 254 nm; solvent, water–MeOH (1 : 1); t_R 22.3 min (**8a**), 34.5 min (**8b**)].

8a: Colorless oil. High-resolution MS *m/z*: 524.1681 Calcd for $C_{28}H_{28}O_{10}$ (M^+). Found: 524.1673. MS *m/z*: 524 (M^+), 506, 433, 415, 385, 316, 300, 272, 251, 208. IR ($CHCl_3$): 3600, 3405, 1720, 1605, 1600, 1580 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.70 (1H, dd, J=3.0, 12.1 Hz, $C_{9'}$-H), 3.82 (6H, s, 2 × OCH_3), 3.94 (3H, s, OCH_3), 4.03 (1H, dd, J=5.0, 12.1 Hz, $C_{9'}$-H), 4.24 (1H, ddd, J=2.7, 3.0, 5.0 Hz, $C_{8'}$-H), 4.98 (2H, s, $OC\underline{H}_2Ph$), 5.39 (1H, d, J=2.7 Hz, $C_{7'}$-H), 6.27 (1H, d, J=9.4 Hz, C_3-H), 6.65 (2H, s, $C_{2'}$-H and $C_{6'}$-H), 6.71 (1H, s, C_5-H), 7.27—7.48 (5H, m, aromatic protons), 7.63 (1H, d, J=9.4 Hz, C_4-H), 8.82 (1H, br s, OH).

8b: Colorless oil. High-resolution MS *m/z*: 524.1681 Calcd for $C_{28}H_{28}O_{10}$ (M^+). Found: 524.1676. MS *m/z*: 524 (M^+), 506, 433, 415, 385, 316, 300, 272, 251, 208. IR ($CHCl_3$): 3600, 3405, 1715, 1605, 1600, 1580 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.47 (1H, dd, J=2.7, 12.1 Hz, $C_{9'}$-H), 3.81 (6H, s, 2 × OCH_3), 3.93 (1H, dd, J=3.0, 12.1 Hz, $C_{9'}$-H), 3.94 (3H, s, OCH_3), 4.01 (1H, ddd, J=2.7, 3.0, 8.4 Hz, $C_{8'}$-H), 4.99 (2H, s, $OC\underline{H}_2Ph$), 5.23 (1H, d, J=8.4 Hz, $C_{7'}$-H), 6.25 (1H, d, J=9.4 Hz, C_3-H), 6.67 (2H, s, $C_{2'}$-H and $C_{6'}$-H), 6.70 (1H, s, C_5-H), 7.28—7.47 (5H, m, aromatic protons), 7.60 (1H, d, J=9.4 Hz, C_4-H), 9.28 (1H, br s, OH).

Aquillochin (1)——A mixture of **8a, b** (135 mg), 35% HCl (2.0 ml), and acetic acid (2.0 ml) was heated at 60 °C for 15 min. The reaction mixture was poured into ice-water and extracted with AcOEt. The AcOEt layer was washed with water, dried over Na_2SO_4, and evaporated. The residue was purified by preparative TLC ($CHCl_3$–acetone (5 : 1)) to

afford a solid, which was recrystallized from MeOH to give colorless needles (**1**, 38 mg, 35%). mp 238 °C (lit.,[4] mp 255 °C). High-resolution MS *m/z*: 416.1106 Calcd for $C_{21}H_{20}O_9$ (M^+). Found: 416.1110. MS *m/z*: 416 (M^+), 398, 249, 210, 208, 193, 182, 180, 167, 154, 149. IR (KBr): 3420, 1710, 1690, 1610, 1575 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 3.42 (1H, dd, J=4.4, 12.4 Hz, $C_{9'}$-H), 3.68 (1H, br d, J=12.4 Hz, $C_{9'}$-H), 3.77 (6H, s, 2 × OCH_3), 3.79 (3H, s, OCH_3), 4.37 (1H, m, $C_{8'}$-H), 4.97 (1H, d, J=8.1 Hz, $C_{7'}$-H), 5.08 (1H, br t, J=5.0 Hz, CH_2OH), 6.34 (1H, d, J=9.4 Hz, C_3-H), 6.76 (2H, s, $C_{2'}$-H and $C_{6'}$-H), 6.91 (1H, s, C_5-H), 7.96 (1H, d, J=9.4 Hz, C_4-H), 8.57 (1H, br s, OH). ^{13}C-NMR[9] (pyridine-d_5) δ: 160.7 (C-2), 149.3 (C-3′ and C-5′), 146.4 (C-6), 144.4 (C-4), 139.3 (C-9), 138.5 (C-7), 133.1 (C-8), 126.4 (C-1′), 113.8 (C-3), 111.9 (C-10), 106.4 (C-2′ and C-6′), 101.1 (C-5), 79.9 (C-8′), 77.8 (C-7′), 60.7 (C-9′), 56.4 (2 × OCH_3), 56.2 (OCH_3).

Condensation of 5 with 9 (Formation of 10)——A solution of **5** (1.16 g) in acetonitrile (8.0 ml) was added dropwise to a mixture of **9**[2d] (690 mg) and *tert*-BuOK (410 mg) in acetonitrile (20 ml). The mixture was stirred at room temperature for 30 min. The reaction mixture was poured into ice-water and extracted with AcOEt. The AcOEt layer was washed with water, dried over Na_2SO_4, and evaporated. The crude product was purified by column chromatography on silica gel ($CHCl_3$–acetone (20 : 1)) to give a colorless oil (**10**, 1.28 g, 81%). FAB-MS *m/z*: 655 ($C_{37}H_{34}O_{11}$ + H)$^+$. IR ($CHCl_3$): 1735, 1680, 1590 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.15 (3H, t, J=7.1 Hz, OCH_2CH_3), 3.71 (3H, s, OCH_3), 3.81 (6H, s, 2 × OCH_3), 4.18 (2H, q, J=7.1 Hz, OCH_2CH_3), 5.11 (2H, s, OCH_2Ph), 5.18 (2H, s, OCH_2Ph), 5.86 (1H, s, $C_{8'}$-H), 6.34 (1H, d, J=9.4 Hz, C_3-H), 6.63 (1H, s, C_5-H), 7.35 (2H, s, $C_{2'}$-H and $C_{6'}$-H), 7.26—7.48 (10H, m, aromatic protons), 7.57 (1H, d, J=9.4 Hz, C_4-H).

Catalytic Reduction of 10 (Formation of 11)——A suspension of **10** (115 mg) and 5% Pd–C (18 mg) in MeOH (10 ml) was stirred under a hydrogen atmosphere until the H_2 uptake had ceased. The catalyst was filtered off and the filtrate was evaporated to give an oil. The crude product was purified by preparative TLC ($CHCl_3$–MeOH (10 : 1)) and then recrystallized from MeOH to give colorless prisms (**11**, 75 mg, 90%). mp 216 °C. FAB-MS *m/z*: 475 ($C_{23}H_{22}O_{11}$ + H)$^+$. IR (KBr): 3440, 1720, 1610, 1580 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.24 (3H, t, J=7.1 Hz, OCH_2CH_3), 3.82 (3H, s, OCH_3), 3.97 (6H, s, 2 × OCH_3), 4.30 (2H, q, J=7.1 Hz, OCH_2CH_3), 5.74 (1H, s, $C_{8'}$-H), 6.33 (1H, d, J=9.4 Hz, C_3-H), 6.45 (1H, s, C_5-H), 7.47 (2H, s, $C_{2'}$-H and $C_{6'}$-H), 7.56 (1H, d, J=9.4 Hz, C_4-H), 8.40 (1H, br s, OH).

Reduction of 11 with Lithium Borohydride (Formation of 12a, b)——$LiBH_4$ (110 mg) was added gradually to a solution of **11** (500 mg) in dry THF (10 ml) at 0 °C and the resulting mixture was stirred at the same temperature for 10 min. The reaction mixture was poured into ice-water and extracted with AcOEt. The AcOEt layer was washed with water, dried over Na_2SO_4, and evaporated to give an oil. The oil was separated by column chromatography on silica gel ($CHCl_3$–MeOH (10 : 1)), yielding a pure product (**12a**, 204 mg, 45%) and a crude material (**12b**). The crude substance (**12b**) was purified by preparative TLC ($CHCl_3$–MeOH (10 : 1)) to give a pure product (**12b**, 18 mg, 4%).

12a: Amorphous solid. TLC (silica gel/$CHCl_3$–MeOH (10 : 1), Rf=0.35). FAB-MS *m/z*: 435 ($C_{21}H_{22}O_{10}$ + H)$^+$. IR (KBr): 3420, 1710, 1620, 1580 cm^{-1}. ^{1}H-NMR (acetone-d_6) δ: 3.60 (1H, dd, J=3.7, 11.4 Hz, $C_{9'}$-H), 3.80 (6H, s, 2 × OCH_3), 3.91 (3H, s, OCH_3), 3.96 (1H, dd, J=7.4, 11.4 Hz, $C_{9'}$-H), 4.23 (1H, ddd, J=3.7, 3.7, 7.4 Hz, $C_{8'}$-H), 5.20 (1H, d, J=3.7 Hz, $C_{7'}$-H), 6.32 (1H, d, J=9.4 Hz, C_3-H), 6.78 (2H, s, $C_{2'}$-H and $C_{6'}$-H), 6.81 (1H, s, C_5-H), 7.15 (1H, br s, OH), 7.87 (1H, d, J=9.4 Hz, C_4-H).

12b: Amorphous solid. TLC (silica gel/$CHCl_3$–MeOH (10 : 1), Rf=0.38). FAB-MS *m/z*: 435 ($C_{21}H_{22}O_{10}$ + H)$^+$. IR (KBr): 3420, 1715, 1620, 1570 cm^{-1}. ^{1}H-NMR (acetone-d_6) δ: 3.47 (1H, dd, J=5.7, 12.1 Hz, $C_{9'}$-H), 3.75 (1H, dd, J=3.0, 12.1 Hz, $C_{9'}$-H), 3.82 (6H, s, 2 × OCH_3), 3.93 (3H, s, OCH_3), 4.04 (1H, ddd, J=3.0, 5.7, 7.7 Hz, $C_{8'}$-H), 5.06 (1H, d, J=7.7 Hz, $C_{7'}$-H), 6.33 (1H, d, J=9.4 Hz, C_3-H), 6.81 (2H, s, $C_{2'}$-H and $C_{6'}$-H), 6.82 (1H, s, C_5-H), 7.21 (1H, br s, OH), 7.87 (1H, d, J=9.4 Hz, C_4-H).

Cleomiscosin D (2)——A mixture of **12a, b** (185 mg), 35% HCl (2.0 ml), and acetic acid (2.0 ml) was heated at 60 °C for 10 min. The reaction mixture was worked up according to the same procedure as described for **1** to give an oil. The crude substance was purified by preparative TLC ($CHCl_3$–MeOH (10 : 1)) to afford a solid. The solid was recrystallized from MeOH to give colorless prisms (**2**, 25 mg, 14%). mp 258 °C (lit.,[5] mp 243—246 °C). High-resolution MS *m/z*: 416.1106 Calcd for $C_{21}H_{20}O_9$ (M^+). Found: 416.1107. MS *m/z*: 416 (M^+), 398, 249, 210, 208, 193, 182, 180, 167, 154, 149. IR (KBr): 3420, 1715, 1690, 1610, 1580 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 3.39 (1H, dd, J=4.4, 12.4 Hz, $C_{9'}$-H), 3.63 (1H, br d, J=12.4 Hz, $C_{9'}$-H), 3.78 (6H, s, 2 × OCH_3), 3.85 (3H, s, OCH_3), 4.37 (1H, m, $C_{8'}$-H), 4.96 (1H, d, J=8.1 Hz, $C_{7'}$-H), 5.04 (1H, br s, OH), 6.32 (1H, d, J=9.4 Hz, C_3-H), 6.77 (2H, s, $C_{2'}$-H and $C_{6'}$-H), 6.95 (1H, s, C_5-H), 7.96 (1H, d, J=9.4 Hz, C_4-H), 8.61 (1H, br s, OH). ^{13}C-NMR (pyridine-d_5) δ: 160.7 (C-2), 149.3 (C-3′ and C-5′), 146.2 (C-6), 144.3 (C-4), 139.4 (C-9), 138.6 (C-7), 133.1 (C-8), 126.4 (C-1′), 113.7 (C-3), 111.7 (C-10), 106.4 (C-2′ and C-6′), 101.1 (C-5), 80.1 (C-8′), 77.4 (C-7′), 61.0 (C-9′), 56.3 (2 × OCH_3), 56.1 (OCH_3).

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References and Notes

1) Because of our interest in the biological activities of coumarinolignoids, we have developed convenient syntheses

of cleomiscosin A,[2a] cleomiscosin B,[2b] daphneticin, [2c] and propacin.[2d]

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9) The peak at the C-4′ position was not determined because it overlapped with solvent (pyridine) peaks.