Isolation, Total Synthesis, and Relative Stereochemistry of a Dihydrofurocoumarin from *Dorstenia contrajerva*

Ricardo Tovar-Miranda,[†] Raúl Cortés-García,[†] Norma F. Santos-Sánchez,[†] and Pedro Joseph-Nathan*[,‡]

Instituto de Ciencias Básicas, Universidad Veracruzana, Apartado Postal 575, Xalapa, Ver., 91000 México, and Departamento de Química del Centro de Investigación y de Estudios Avanzados, Instituto Politécnico Nacional, Apartado 14-740, México, D.F., 07000 México

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The roots of *Dorstenia contrajerva* afforded the dihydrofurocoumarin **1b** whose identity was determined from NMR spectral data of the derived acetate **7b** combined with the total syntheses of **1a** and **1b**, which were carried out in five steps with 19% overall yield, starting from 2,3-dihydro-2-isopropenyl-6-methoxybenzofuran (**2**). The relative stereochemistry of **7b** was determined from a single-crystal X-ray diffraction study as (2*S**,1′*S**)-2,3-dihydro-2-(1′-hydroxy-1′-acetyloxymethylethyl)-7*H*-furo[3,2g][1]benzopyran-7-one.

As part of our work on the isolation and identification of plant metabolites, we have studied the roots of *Dorstenia contrajerva* L. (Moraceae), a plant from the traditional medicine of southeastern Mexico, used mainly as a rattlesnake bite tonic. The chromatographic separation of the chloroform extracts resulted in the isolation of the 5-methoxyfurocoumarin bergapten,[1,2] and an insoluble amorphous solid named dorsteniol, which was acetylated. The structure of the derived acetate was deduced from the ^{1}H and ^{13}C NMR data as **7a** or **7b**.

A literature search showed that an acetate[3] (**7a** or **7b**) was prepared from prandiol (**1a** or **1b**), which was isolated from the roots of *Prangos biebersteinii*. The spectral data of prandiol acetate and of dorsteniol acetate revealed that these two substances are different. The authors[3] also prepared the derived diacetate **8a** or **8b**, but they did not report specific rotations for the natural product or its derivatives. Another study showed that the seeds of *Apium graveolens*[4] have afforded an optical isomer of prandiol, with this conclusion being deduced from the large difference in melting points. In the latter case the monoacetate and diacetate derivatives were not prepared, but the specific rotation for the coumarin isolated from the *Apium* species was reported.

The main spectral difference observed by comparing the ^{1}H NMR spectrum of the monoacetate derived from the furocoumarin from *Prangos* species with that prepared by our group from the furocoumarin from *Dorstenia* species is found for the H-2′ methylene signal, which, in the case of prandiol monoacetate,[3] appears at 100 MHz as a singlet at δ 4.17 ppm, while in dorsteniol monoacetate it is observed at 300 MHz as an AB system (δ_A = 4.34, δ_B = 4.12 ppm, J = 11.4 Hz).

To gain confirmation that the furocoumarins from the *Prangos* and *Apium* species are indeed stereoisomers, we describe herein the total synthesis of both isomers and further compare the synthetic sample with the constituent of the *Dorstenia* species. The relative stereochemistry of the natural and synthetic compounds follows from a single-crystal X-ray study of dorsteniol acetate (**7b**).

* To whom correspondence should be addressed. Tel.: 525-7477112. Fax: 525-7477113. E-mail: pjoseph@nathan.chem.cinvestav.mx.
† Universidad Veracruzana.
‡ Instituto Politécnico Nacional.

Results and Discussion

We envisaged that olefin **2** would be a suitable starting material[5,6] for the synthesis of **1a** and **1b**, as shown in Scheme 1. Treatment of **2** with ADmix-α in *tert*-butyl alcohol−water[7] at 0 °C gave a diastereomeric mixture of diols **3a** and **3b**, in 85% yield. Because it was not possible to separate the diastereoisomers, the mixture was treated with anhydrous acetone in the presence of *p*-toluenesulfonic acid[8] to afford the corresponding mixture of ketals (**4a**,**4b**) in 90% yield. At this point, it was possible to separate the diastereoisomeric mixture by column chromatography and to establish that the ketals **4a** and **4b** were obtained in a 3:2 ratio, respectively. A similar number of ^{1}H and ^{13}C NMR signals and multiplicities were observed for both substances **4a** (R_f 0.43) and **4b** (R_f 0.34), but they exhibited differences in their chemical shift values, thus confirming that these compounds have the same structure but different stereochemistry. Acid hydrolysis of **4a** and of **4b** gave pure **3a** and **3b**, respectively.

Each ketal (**4a**,**4b**) was subjected to the following sequence of reactions. Treatment of **4a** or **4b** with ethanethiol lithium salt in *N*,*N*-dimethylformamide[9] at 85 °C gave the desired phenols **5a** or **5b** in 80% yield. Compound **5a** was treated[10,11] with ethyl propiolate and $ZnCl_2$ at 90 °C to yield ketalcoumarin **6a** and coumarin **1a**, while under the same reaction conditions the phenol **5b** gave only **1b**.

The UV and IR spectra of **1a** and **1b** showed characteristic bands of a coumarin moiety,[2,12] while in the mass spectra of **1a** and **1b** the $[M]^+$ was observed at *m*/*z* 262 in accordance with the molecular formula $C_{14}H_{14}O_5$. The ^{1}H NMR spectra in acetone-d_6 showed differences for the H-2′ methylene AB system signals: for **1a**, at 3.60 and 3.52 ppm for H-2′a and H-2′b, respectively, and for **1b**, at 3.71 and 3.57 ppm. These differences remained when the solvent was changed to methanol-d_4 for **1a**, at 3.56 and 3.50 ppm for H-2′a and H-2′b, respectively, and for **1b**, at 3.73 and 3.51 ppm. Spectral measurements in both solvents were necessary because the ^{1}H NMR spectrum of the coumarin from *P. biebersteinii* was recorded[3] in methanol-d_4, while that for the coumarin from *A. graveolens*[4] was recorded in acetone-d_6.

Refluxing of both **1a** and **1b** in acetic anhydride and pyridine gave the monoacetate derivatives (**7a**, **7b**) and diacetate derivatives (**8a**, **8b**), respectively. The ^{1}H NMR spectra of monoacetates **7a** and **7b** showed differences for

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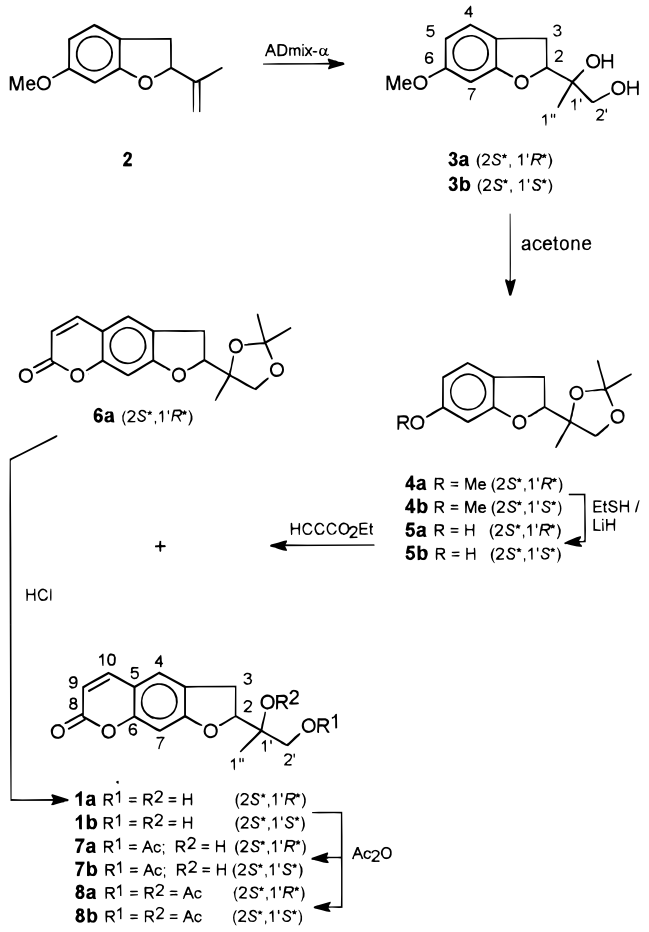
Scheme 1. Synthetic Route for **1a** and **1b**



the H-2′ signals. For **7a** the AB system appeared at 4.18 and 4.16 ppm, while for **7b**, it appeared at 4.34 and 4.12 ppm. In the case of the diacetate derivatives **8a** and **8b** also a difference for the H-2′ protons was observed as AB systems, for **8a** at 4.69 and 4.51 ppm and for **8b** at 4.54 and 4.50 ppm.

Comparison of ^{1}H NMR spectra of the synthetic dihydrofurocoumarins and their monoacetate and diacetate derivatives with those reported in the literature from *Prangos*,[3] *Apium*,[4] and the one isolated by us from *Dorstenia* species, revealed that **1a** is identical to that isolated from *P. biebersteinii*, while **1b** is identical to that isolated from *A. graveolens* and *D. contrajerva*.

Because a monoacetylation of the dihydrofurocoumarin isolated from *D. contrajerva* provided suitable crystals for a single-crystal X-ray diffraction study, we determined the relative configuration of the two chiral carbons as 2*S**,1′*S**, as shown in Figure 1, where it was observed that the hydrogen at the atom labeled as C-12 and the methyl group at the atom labeled as C-13 have the α-orientation, and therefore the *S** relative configuration is observed for both chiral centers. The experimentally refined final fractional atomic coordinates are listed in Table 1. It further follows that **1b**, isolated from *Apium* species, has the same configuration as the compound isolated by us, while the dihydrofurocoumarin isolated from *Prangos* species has the 2*S**,1′*R** configuration.

Experimental Section

General Experimental Procedures. Organic layers were dried using anhydrous Na_2SO_4. Columns for chromatographic separations were packed with Merck Si gel 60 (230−400 mesh ASTM). Melting points were measured on a Melt-Temp II and are uncorrected. IR spectra were recorded on a Perkin−Elmer 16F PC FT-IR spectrophotometer. UV spectra were recorded on a Perkin−Elmer Lambda 2S spectrometer. ^{1}H and ^{13}C NMR measurements were performed on a Varian XL-300GS spectrometer from $CDCl_3$ solutions containing TMS as internal standard. MS were obtained on a Hewlett−Packard 5989A spectrometer at 20 eV. HRMS and FABMS were measured on a JEOL JMS−SX 102A spectrometer.

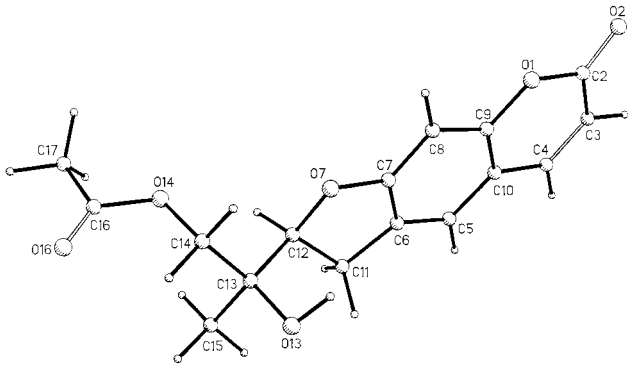


Figure 1. X-ray crystal structure of **7b** showing the crystallographic numbering.

Table 1. Experimentally Refined Final Fractional Atomic Coordinates (× 10^4) of **7b**[a]

atom	*x*	*y*	*z*
O-1	3901 (4)	6309 (4)	10236 (1)
C-2	3790 (6)	6024 (6)	10710 (1)
O-2	3749 (5)	4522 (4)	10838 (1)
C-3	3717 (7)	7519 (6)	11009 (1)
C-4	3724 (7)	9129 (6)	10830 (1)
C-5	3758 (6)	11050 (5)	10130 (1)
C-6	3775 (7)	11185 (5)	9652 (1)
C-7	3856 (6)	9708 (6)	9381 (1)
O-7	3871 (4)	10027 (4)	8913 (1)
C-8	3907 (6)	8050 (6)	9564 (1)
C-9	3884 (6)	7942 (5)	10048 (1)
C-10	3812 (6)	9402 (5)	10337 (1)
C-11	3761 (7)	12718 (6)	9332 (1)
C-12	3365 (7)	11873 (6)	8854 (1)
C-13	4569 (6)	12586 (6)	8447 (1)
O-13	6684 (5)	12569 (5)	8531 (1)
H-13	6916 (79)	11459 (64)	8692 (15)
C-14	4219 (7)	11514 (7)	8003 (1)
O-14	2102 (5)	11546 (5)	7891 (1)
C-15	4008 (8)	14480 (6)	8369 (2)
C-16	1538 (8)	12201 (7)	7484 (2)
O-16	2693 (6)	12732 (8)	7205 (1)
C-17	−701 (8)	12231 (9)	7444 (2)

[a] Estimated standard deviations in the least significant digits are shown in parentheses.

Plant Material. *D. contrajerva* L. was collected at Barranca de Teocelo (Texolo), Municipio de Xico, Veracruz, México (elevation 1150 m, latitude 19° 24′ north, 97° 00′ west) in August 1988. The species was identified by J. I. Calzada of the Herbarium of Instituto de Ecología A. C., Xalapa, Veracruz, México., where voucher specimen no. 99132 has been deposited.

Extraction and Isolation. Air-dried roots (1.35 kg) of *D. contrajerva* were extracted with hexane (3.0 L) and $CHCl_3$ (3.0 L), evaporated to dryness to afford 11.5 and 25.0 g of brown viscous oils, respectively. A 10-g aliquot of the $CHCl_3$ extract was chromatographed on a Si gel column eluting with hexane−EtOAc to give 200 mg of bergapten[1,2] and 35 mg of an insoluble amorphous solid that could not be further purified. The solid was dissolved in pyridine (1 mL) and Ac_2O (1 mL). The reaction mixture was stored at room temperature for 12 h. After the usual workup, the residue was crystallized from $CHCl_3$−hexane to give **7b** (30 mg, 75%) as white prisms: mp 178−180 °C; $[\alpha]^{25}$ +45° (*c* 1, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ)

203 (4.22), 222 (3.95), 334 (4.19) nm; IR (KBr) ν_{max} 3320, 1730, 1626, 1568, 1496, 1130 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) 7.60 (1H, d, J = 9.5 Hz, H-10), 7.24 (1H, s, H-4), 6.75 (1H, s, H-7), 6.23 (1H, d, J = 9.5 Hz, H-9), 4.89 (1H, t, J = 9.0 Hz, H-2), 4.34 (1H, d, J = 11.4 Hz, H-2′a), 4.12 (1H, d, J = 11.4 Hz, H-2′b), 3.36 (1H, ddd, J = 16.0, 9.0, 1.4 Hz, H-3a), 3.20 (1H, dd, J = 16.0, 9.0 Hz, H-3b), 2.14 (3H, s, $COCH_3$), 1.63 (1H, br s, OH), 1.25 (3H, s, CH_3-1″); ^{13}C NMR ($CDCl_3$, 75.4 MHz) 170.92 (s, $COCH_3$), 162.93 (s, C-7a), 161.37 (s, C-8), 155.59 (s, C-6), 143.63 (d, C-10), 124.63 (s, C-3a), 123.40 (d, C-4), 112.91 (s, C-5), 112.38 (d, C-9), 98.10 (d, C-7), 87.71 (d, C-2), 72.63 (s, C-1′), 68.38 (t, C-2′), 29.02 (t, C-3), 20.89 (q, $COCH_3$), 20.22 (q, C-1″); EIMS m/z 304 $[M]^+$ (42), 188 (98), 187 (100), 117 (19); HRFABMS m/z 305.1019 (calcd for $C_{16}H_{16}O_6$ $[M + H]^+$ 305.1025).

Dihydroxylation of 2. A mixture of ADmix-α (3.67 g), *tert*-butyl alcohol (13.1 mL) and H_2O (13.1 mL) was stirred at room temperature for 30 min, then cooled to 0 °C, and **2**[5,6] (500 mg 2.6 mmol) was added. The mixture was stirred for 24 h at room temperature and extracted with EtOAc. The organic layer was dried and evaporated under vacuum to give a mixture of **3a** and **3b** (520 mg, 85%): UV (EtOH) λ_{max} (log ϵ) 201 (4.59), 287 (3.60) nm; IR ($CHCl_3$) ν_{max} 3630, 1500, 1142 cm^{-1}; EIMS m/z 224 $[M]^+$ (91), 193 (18), 149 (100), 75 (31).

Acetonide of 3a and 3b. A mixture of **3a** and **3b** (2.77 g, 12.3 mmol) dissolved in anhydrous Me_2CO (30 mL) in the presence of a catalytic amount of *p*-toluenesulfonic acid was refluxed for 3 h. The reaction mixture was concentrated to a small volume under vacuum, extracted with Et_2O, washed with H_2O, and dried and evaporated to give 2.94 g (90% yield) of a yellow oil that was purified by flash column chromatography eluting with petroleum ether−EtOAc (99:1) to give **4a** (1.33 g, R_f 0.43, hexane−EtOAc 95:5) and **4b** (990 mg, R_f 0.34, hexane−EtOAc 95:5).

Ketal 4a: white prisms; mp 57−58 °C; UV (EtOH) λ_{max} (log ϵ) 202 (4.58), 222 (3.79), 288 (3.69) nm; IR (KBr) ν_{max} 1596, 1500, 1198 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) 7.01 (1H, d, J = 8.0 Hz, H-4), 6.38 (1H, dd, J = 8.0, 2.3 Hz, H-5), 6.35 (1H, d, J = 2.3 Hz, H-7), 4.76 (1H, dd, J = 9.7, 7.7 Hz, H-2), 4.15 (1H, d, J = 8.8 Hz, H-2′a), 3.79 (1H, d, J = 8.8 Hz, H-2′b), 3.74 (3H, s, OCH_3), 3.18 (1H, ddd, J = 16.1, 9.7, 0.8 Hz, H-3a), 3.09 (1H, ddd, J = 16.1, 7.7, 1.0 Hz, H-3b), 1.42 (3H, s, CH_3-*gem*), 1.41 (3H, s, CH_3-*gem*), 1.25 (3H, s, CH_3-1″); ^{13}C NMR ($CDCl_3$, 75.4 MHz) 160.90 (s, C-6), 160.30 (s, C-7a), 124.69 (d, C-4), 118.60 (s, C-3a), 109.82 (s, C−O_2), 105.97 (d, C-5), 95.99 (d, C-7), 85.79 (d, C-2), 81.84 (s, C-1′), 72.72 (t, C-2′), 55.41 (q, OCH_3), 30.09 (t, C-3), 27.22 (q, CH_3-*gem*), 26.68 (q, CH_3-*gem*), 19.10 (q, C-1″); EIMS m/z 264 $[M]^+$ (64), 148 (45), 115 (100), 43 (24); HRFABMS m/z 264.1365 (calcd for $C_{15}H_{20}O_4$ $[M]^+$ 264.1362).

Ketal 4b: colorless oil; UV (EtOH) λ_{max} (log ϵ) 200 (4.62), 222 (3.78), 287 (3.60) nm; IR ($CHCl_3$) ν_{max} 1596, 1498, 1196 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) 7.00 (1H, dd, J = 7.8, 1.0 Hz, H-4), 6.40 (1H, d, J = 2.3 Hz, H-7), 6.38 (1H, dd, J = 7.8, 2.3 Hz, H-5), 4.73 (1H, dd, J = 9.6, 8.2 Hz, H-2), 4.08 (1H, d, J = 8.8 Hz, H-2′a), 3.78 (1H, d, J = 8.8 Hz, H-2′b), 3.74 (3H, s, OCH_3), 3.15 (1H, dd, J = 15.3, 9.6 Hz, H-3a), 3.06 (1H, ddd, J = 15.3, 8.2, 1.0 Hz, H-3b), 1.42 (3H, s, CH_3-*gem*), 1.39 (3H, s, CH_3-*gem*), 1.36 (3H, s, CH_3-1″); ^{13}C NMR ($CDCl_3$, 75.4 MHz) 161.03 (s, C-6), 160.30 (s, C-7a), 124.67 (d, C-4), 118.41 (s, C-3a), 110.19 (s, C−O_2), 105.86 (d, C-5), 96.02 (d, C-7), 87.03 (d, C-2), 82.36 (s, C-1′), 71.04 (t, C-2′), 55.43 (q, OCH_3), 30.62 (t, C-3), 26.91 (q, CH_3-*gem*), 26.65 (q, CH_3-*gem*), 22.19 (q, C-1″); EIMS m/z 264 $[M]^+$ (66), 148 (62), 115 (100), 43 (22); HRFABMS m/z 264.1365 (calcd for $C_{15}H_{20}O_4$ $[M]^+$ 264.1362).

Hydrolysis of Ketal 4a. To a solution of **4a** (100 mg) in MeOH (10 mL) was added 5% HCl (0.5 mL). The reaction was stirred at 50 °C for 90 min, concentrated to a small volume under vacuum, extracted with CH_2Cl_2, washed with H_2O, dried, and evaporated to give **3a** (76 mg, 90%) as white prisms: mp 86−88 °C; ^1H NMR ($CDCl_3$, 300 MHz) 7.02 (1H, d, J = 8.1 Hz, H-4), 6.39 (1H, dd, J = 8.1, 2.3 Hz, H-5), 6.35 (1H, d, J = 2.3 Hz, H-7), 4.79 (1H, dd, J = 9.4, 8.4 Hz, H-2), 3.74 (1H, d, J = 11.2 Hz, H-2′a), 3.74 (3H, s, OCH_3), 3.50 (1H, d, J = 11.2 Hz, H-2′b), 3.17 (1H, dd, J = 16.0, 8.4 Hz, H-3a), 3.10 (1H, dd, J = 16.0, 9.4 Hz, H-3b), 2.91 (2H, br s, OH), 1.16 (3H, s, CH_3-1″); ^{13}C NMR ($CDCl_3$, 75.4 MHz) 160.48 (s, C-6), 160.26 (s, C-7a), 124.82 (d, C-4), 118.74 (s, C-3a), 106.13 (d, C-5), 96.12 (d, C-7), 86.13 (d, C-2), 73.76 (s, C-1′), 66.96 (t, C-2′) 55.48 (q, OCH_3), 29.61 (t, C-3), 19.00 (q, C-1″); HRFABMS m/z 225.1119 (calcd for $C_{12}H_{16}O_4$ $[M + H]^+$ 225.1127).

Hydrolysis of Ketal 4b. Using the previous procedure, the hydrolysis of ketal **4b** (100 mg) gave **3b** (77 mg, 91%) as white prisms: mp 83−85 °C; ^1H NMR ($CDCl_3$, 300 MHz) 7.04 (1H, d, J = 8.1 Hz, H-4), 6.41 (1H, dd, J = 8.1, 2.3 Hz, H-5), 6.37 (1H, d, J = 2.3 Hz, H-7), 4.80 (1H, t, J = 9.1 Hz, H-2), 3.78 (1H, d, J = 11.4 Hz, H-2′a), 3.75 (3H, s, OCH_3), 3.56 (1H, d, J = 11.4 Hz, H-2′b), 3.21 (1H, ddd, J = 15.1, 9.1, 1.1 Hz, H-3a), 3.07 (1H, dd, J = 15.1, 9.1 Hz, H-3b), 2.60 (2H, br s, OH), 1.15 (3H, s, CH_3-1″); ^{13}C NMR ($CDCl_3$, 75.4 MHz) 160.31 (s, C-6), 160.27 (s, C-7a), 124.87 (d, C-4), 118.50 (s, C-3a), 106.34 (d, C-5), 96.16 (d, C-7), 88.60 (d, C-2), 73.17 (s, C-1′), 68.73 (t, C-2′), 55.52 (q, OCH_3), 29.82 (t, C-3), 19.61 (q, C-1″); HRFABMS m/z 224.1052 (calcd for $C_{12}H_{16}O_4$ $[M]^+$ 224.1049).

Demethylation of 4a. A mixture of LiH (944 mg, 118.9 mmol) and anhydrous DMF (20 mL) under a nitrogen atmosphere was cooled to 0 °C, then a solution of EtSH (8.81 mL, 118.9 mmol) in anhydrous DMF (2 mL) was added dropwise. The reaction mixture was warmed to room temperature for 15 min, and **4a** (900 mg, 3.4 mmol) in anhydrous DMF (6 mL) was added. The reaction was stirred for 24 h at 85 °C, acidified with 5% HCl, extracted with Et_2O, washed with H_2O, and dried and evaporated to give a solid residue, which was purified by column chromatography eluting with petroleum ether−EtOAc (8:2) to give **5a** (680 mg, 80%) as white prisms: mp 107−108 °C; UV (EtOH) λ_{max} (log ϵ) 202 (4.51), 222 (3.79), 289 (3.68) nm; IR (KBr) ν_{max} 3396, 1506, 1468, 1140 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) 6.95 (1H, dd, J = 7.6, 0.9 Hz, H-4), 6.30 (1H, dd, J = 7.6, 2.3 Hz, H-5), 6.28 (1H, d, J = 2.3 Hz, H-7), 5.69 (1H, br s, OH), 4.76 (1H, dd, J = 9.5, 7.5 Hz, H-2), 4.16 (1H, d, J = 8.8 Hz, H-2′a), 3.81 (1H, d, J = 8.8 Hz, H-2′b), 3.16 (1H, dd, J = 16.0, 9.5 Hz, H-3a), 3.06 (1H, ddd, J = 16.0, 7.5, 0.9 Hz, H-3b), 1.44 (3H, s, CH_3-*gem*), 1.42 (3H, s, CH_3-*gem*), 1.26 (3H, s, CH_3-1″); ^{13}C NMR ($CDCl_3$, 75.4 MHz) 160.86 (s, C-7a), 156.20 (s, C-6), 124.90 (d, C-4), 118.51 (s, C-3a), 110.03 (s, C−O_2), 107.33 (d, C-5), 97.50 (d, C-7), 85.84 (d, C-2), 81.99 (s, C-1′), 72.57 (t, C-2′), 30.11 (t, C-3), 27.17 (q, CH_3-*gem*), 26.71 (q, CH_3-*gem*), 19.29 (q, C-1″); EIMS m/z 250 $[M]^+$ (44), 134 (33), 115 (100), 57 (35); HRFABMS m/z 250.1205 (calcd for $C_{14}H_{18}O_4$ $[M]^+$ 250.1205).

Demethylation of 4b. The phenol **5b** was prepared from **4b** (500 mg) in the same way as described above, giving **5b** (378 mg, 80%) as white prisms: mp 120−121 °C; UV (EtOH) λ_{max} (log ϵ) 202 (4.48), 222 (3.82), 289 (3.66) nm; IR (KBr) ν_{max} 3360, 1506, 1464, 1138 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) 6.96 (1H, d, J = 8.0 Hz, H-4), 6.43 (1H, d, J = 2.3 Hz, H-7), 6.31 (1H, dd, J = 8.0, 2.3 Hz, H-5), 5.46 (1H, br s, OH), 4.75 (1H, dd, J = 9.7, 8.1 Hz, H-2), 4.11 (1H, d, J = 8.8 Hz, H-2′a), 3.81 (1H, d, J = 8.8 Hz, H-2′b), 3.15 (1H, dd, J = 15.3, 9.7 Hz, H-3a), 3.03 (1H, ddd, J = 15.3, 8.1, 1.1 Hz, H-3b), 1.43 (3H, s, CH_3-*gem*), 1.40 (3H, s, CH_3-*gem*), 1.36 (3H, s, CH_3-1″); ^{13}C NMR ($CDCl_3$, 75.4 MHz) 161.05 (s, C-7a), 156.24 (s, C-6), 124.88 (d, C-4), 118.27 (s, C-3a), 110.41 (s, C−O_2), 107.20 (d, C-5), 97.49 (d, C-7), 87.11 (d, C-2), 82.56 (s, C-1′), 71.18 (t, C-2′), 30.64 (t, C-3), 26.87 (q, CH_3-*gem*), 26.69 (q, CH_3-*gem*), 21.88 (q, C-1″); EIMS m/z 250 $[M]^+$ (46), 134 (46), 115 (100), 57 (36); HRFABMS m/z 250.1212 (calcd for $C_{14}H_{18}O_4$ $[M]^+$ 250.1205).

Condensation of 5a with Ethyl Propiolate. A mixture of freshly fused zinc chloride (126.5 mg, 0.9 mmol), ethyl propiolate (0.6 mL, 5.52 mmol), and **5a** (155 mg, 0.6 mmol) was heated at 90 °C for 2 h under a nitrogen atmosphere. After being cooled, the brown solid was treated with 5% HCl, extracted with CH_2Cl_2, washed with H_2O, and dried and evaporated to give a yellow solid. The crude residue was purified by column chromatography eluting with petroleum ether−Me_2CO (85:15) to give **6a** (12 mg, 6%). Further elution with petroleum ether−Me_2CO (60:40) afforded **1a** (53 mg, 33%).

Ketalcoumarin 6a: white prisms; mp 143−145 °C; UV (EtOH) λ_{max} (log ϵ) 204 (4.64), 223 (3.56), 333 (4.13) nm; IR

(KBr) ν_{max} 1726, 1628, 1574, 1122 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) 7.59 (1H, d, J = 9.5 Hz, H-10), 7.22 (1H, s, H-4), 6.71 (1H, s, H-7), 6.21 (1H, d, J = 9.5 Hz, H-9), 4.88 (1H, dd, J = 9.1, 7.5 Hz, H-2), 4.15 (1H, d, J = 8.9 Hz, H-2′a), 3.83 (1H, d, J = 8.9 Hz, H-2′b), 3.31 (1H, ddd, J = 16.5, 9.1, 1.2 Hz, H-3a), 3.25 (1H, ddd, J = 16.5, 7.5, 1.2 Hz, H-3b), 1.42 (3H, s, CH_3-*gem*), 1.41 (3H, s, CH_3-*gem*), 1.26 (3H, s, CH_3-1″); ^{13}C NMR ($CDCl_3$, 75.4 MHz) 163.26 (s, C-8), 161.29 (s, C-7a), 155.76 (s, C-6), 143.55 (d, C-10), 124.67 (s, C-3a), 123.29 (d, C-4), 112.79 (s, C-5), 112.31 (d, C-9), 110.09 (s, C−O_2), 97.95 (d, C-7), 86.74 (d, C-2), 81.43 (s, C-1′), 72.71 (t, C-2′), 29.53 (t, C-3), 27.26 (q, CH_3-*gem*), 26.41 (q, CH_3-*gem*), 19.01 (q, C-1″); EIMS *m*/*z* 302 [M]$^+$ (44), 187 (10), 115 (100), 43 (13); HRFABMS *m*/*z* 303.1240 (calcd for $C_{17}H_{18}O_5$ [M + H]$^+$ 303.1232).

Dihydrofurocoumarin 1a: white prisms; mp 157−158 °C; UV (EtOH) λ_{max} (log ϵ) 203 (4.53), 222 (3.96), 335 (4.01) nm; IR (KBr) ν_{max} 3426, 1718, 1628, 1568, 1128 cm^{-1}; ^{1}H NMR (Me_2-CO-d_6, 300 MHz) 7.84 (1H, d, J = 9.5 Hz, H-10), 7.42 (1H, d, J = 1.3 Hz, H-4), 6.65 (1H, s, H-7), 6.15 (1H, d, J = 9.5 Hz, H-9), 5.01 (1H, dd, J = 9.6, 7.6 Hz, H-2), 3.60 (1H, d, J = 11.0 Hz, H-2′a), 3.52 (1H, d, J = 11.0 Hz, H-2′b), 3.41 (1H, ddd, J = 16.2, 7.6, 1.3 Hz, H-3a), 3.23 (1H, ddd, J = 16.2, 9.6, 1.0 Hz, H-3b), 2.96 (2H, br s, OH), 1.20 (3H, s, CH_3-1″); ^{1}H NMR (MeOH-d_4, 300 MHz) 7.83 (1H, d, J = 9.3 Hz, H-10), 7.39 (1H, s, H-4), 6.69 (1H, s, H-7), 6.18 (1H, d, J = 9.3 Hz, H-9), 4.96 (1H, dd, J = 9.6, 7.8 Hz, H-2), 4.86 (2H, s, OH) 3.56 (1H, d, J = 11.3 Hz, H-2′a), 3.50 (1H, d, J = 11.3 Hz, H-2′b), 3.37 (1H, ddd, J = 16.2, 7.8, 1.4 Hz, H-3a), 3.22 (1H, ddd, J = 16.2, 9.6, 1.1 Hz, H-3b), 1.21 (3H, s, CH_3-1″); ^{13}C NMR (Me_2CO-d_6, 75.4 MHz) 164.46 (s, C-8), 161.20 (s, C-7a), 156.57 (s, C-6), 144.91 (d, C-10), 126.56 (s, C-3a), 124.68 (d, C-4), 113.36 (s, C-5), 112.42 (d, C-9), 97.75 (d, C-7), 88.14 (d, C-2), 73.76 (s, C-1′), 67.90 (t, C-2′), 29.40 (t, C-3), 19.85 (q, C-1″); ^{13}C NMR (methanol-d_4, 75.4 MHz) 165.13 (s, C-8), 163.70 (s, C-7a), 156.86 (s, C-6), 146.20 (d, C-10), 127.35 (s, C-3a), 124.98 (d, C-4), 114.08 (s, C-5), 112.16 (d, C-9), 98.18 (d, C-7), 88.58 (d, C-2), 74.37 (s, C-1′), 68.06 (t, C-2′), 29.70 (t, C-3), 19.63 (q, C-1″); EIMS *m*/*z* 262 [M]$^+$ (55), 188 (94), 187 (100), 159 (13), 75 (30); HRFABMS *m*/*z* 263.0926 (calcd for $C_{14}H_{14}O_5$ [M + H]$^+$ 263.0919).

Condensation of 5b with Ethyl Propiolate. The furocoumarin **1b** (48 mg, 30%) was obtained from **5b** using the previous procedure as white prisms: mp 185−187 °C; UV (EtOH) λ_{max} (log ϵ) 204 (4.54), 222 (3.72), 335 (4.00) nm; IR (KBr) ν_{max} 3396, 1718, 1628, 1568, 1130 cm^{-1}; ^{1}H NMR (Me_2-CO-d_6, 300 MHz) 7.84 (1H, d, J = 9.5 Hz, H-10), 7.43 (1H, s, H-4), 6.63 (1H, s, H-7), 6.14 (1H, d, J = 9.5 Hz, H-9), 5.01 (1H, dd, J = 9.4, 8.5 Hz, H-2), 3.71 (1H, d, J = 10.6 Hz, H-2′a), 3.57 (1H, d, J = 10.6 Hz, H-2′b), 3.38 (1H, ddd, J = 16.2, 8.5, 1.3 Hz, H-3a), 3.24 (1H, ddd, J = 16.2, 9.4, 0.9 Hz, H-3b), 2.91 (2H, br s, 2OH), 1.18 (3H, s, CH_3-1″); ^{1}H NMR (MeOH-d_4, 300 MHz) 7.84 (1H, d, J = 9.5 Hz, H-10), 7.39 (1H, d, J = 1.4 Hz, H-4), 6.71 (1H, s, H-7), 6.18 (1H, d, J = 9.5 Hz, H-9), 4.97 (1H, t, J = 9.0 Hz, H-2), 4.88 (2H, s, OH) 3.73 (1H, d, J = 10.9 Hz, H-2′a), 3.51 (1H, d, J = 10.9 Hz, H-2′b), 3.34 (1H, ddd, J = 15.6, 9.0, 1.4 Hz, H-3a), 3.22 (1H, ddd, J = 15.6, 9.0, 0.9 Hz, H-3b), 1.18 (3H, s, CH_3-1″); ^{13}C NMR (Me_2CO-d_6, 75.4 MHz) 164.58 (s, C-8), 161.16 (s, C-7a), 156.58 (s, C-6), 144.88 (d, C-10), 126.49 (s, C-3a), 124.58 (d, C-4), 113.29 (s, C-5), 112.38 (d, C-9), 97.73 (d, C-7), 89.06 (d, C-2), 74.00 (s, C-1′), 67.61 (t, C-2′), 29.71 (t, C-3), 20.81 (q, C-1″); ^{13}C NMR (MeOH-d_4, 75.4 MHz) 165.25 (s, C-8), 163.75 (s, C-7a), 156.87 (s, C-6), 146.24 (d, C-10), 127.32 (s, C-3a), 124.91 (d, C-4), 114.04 (s, C-5), 112.13 (d, C-9), 98.25 (d, C-7), 89.16 (d, C-2), 74.66 (s, C-1′), 67.71 (t, C-2′), 29.71 (t, C-3), 20.38 (q, C-1″); EIMS *m*/*z* 262 [M]$^+$ (60), 188 (100), 187 (100), 159 (10), 75 (20); HRFABMS *m*/*z* 263.0925 (calcd for $C_{14}H_{14}O_5$ [M + H]$^+$ 263.0919).

Acetylation of 1a. A solution of **1a** (32 mg, 0.12 mmol) in Ac_2O (0.64 mL) and pyridine (0.5 mL) was refluxed for 1 h, poured over ice, and extracted with EtOAc. After the usual workup, the residue was purified by preparative TLC (petroleum ether−Me_2CO 3:2) to give **7a** (12.2 mg, 33%, R_f 0.26) and **8a** (13.5 mg, 32% R_f 0.41).

Monoacetate 7a: white prisms; mp 124−126 °C; UV (EtOH) λ_{max} (log ϵ) 203 (4.57), 223 (3.91), 335 (4.13) nm; IR (KBr) ν_{max} 3304, 1720, 1630, 1568, 1448, 1126 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) 7.60 (1H, d, J = 9.5 Hz, H-10), 7.24 (1H, t, J = 1.3 Hz, H-4), 6.73 (1H, s, H-7), 6.22 (1H, d, J = 9.5 Hz, H-9), 4.89 (1H, dd, J = 9.5, 7.7 Hz, H-2), 4.18 (1H, d, J = 12.1 Hz, H-2′a), 4.16 (1H, d, J = 12.1 Hz, H-2′b), 3.35 (1H, ddd, J = 16.3, 7.7, 1.3 Hz, H-3a), 3.25 (1H, ddd, J = 16.3, 9.5, 1.0 Hz, H-3b), 1.58 (1H, br s, OH), 2.13 (3H, s, $COCH_3$), 1.25 (3H, s, CH_3-1″); ^{13}C NMR ($CDCl_3$, 75.4 MHz) 171.09 (s, $OCOCH_3$), 162.87 (s, C-7a), 161.25 (s, C-8), 155.73 (s, C-6), 143.53 (d, C-10), 124.56 (s, C-3a), 123.42 (d, C-4), 112.95 (s, C-5), 112.53 (d, C-9), 98.08 (d, C-7), 86.58 (d, C-2), 72.76 (s, C-1′), 68.41 (t, C-2′), 29.09 (t, C-3), 20.80 (q, $COCH_3$), 19.61 (q, C-1″); EIMS *m*/*z* 304 [M]$^+$ (76), 244 (5), 188 (100), 187 (90), 159 (9), 117 (15); HRFABMS *m*/*z* 305.1022 (calcd for $C_{16}H_{16}O_6$ [M + H]$^+$ 305.1025).

Diacetate 8a: white prisms; mp 114−115 °C; UV (EtOH) λ_{max} (log ϵ) 202 (4.48), 222 (3.88), 333 (4.06) nm; IR (KBr) ν_{max} 1750, 1724, 1628, 1574, 1130 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) 7.60 (1H, d, J = 9.5 Hz, H-10), 7.23 (1H, s, H-4), 6.74 (1H, s, H-7), 6.23 (1H, d, J = 9.5 Hz, H-9), 5.31 (1H, t, J = 8.5 Hz, H-2), 4.69 (1H, d, J = 12.1 Hz, H-2′a), 4.51 (1H, d, J = 12.1 Hz, H-2′b), 3.29 (2H, d, J = 8.5 Hz, H-3), 2.10 (3H, s, $COCH_3$), 2.03 (3H, s, $COCH_3$), 1.45 (3H, s, CH_3-1″); ^{13}C NMR ($CDCl_3$, 75.4 MHz) 170.21, 169.81 (s, $COCH_3$), 162.84 (s, C-7a), 161.14 (s, C-8), 155.74 (s, C-6), 143.45 (d, C-10), 124.05 (s, C-3a), 123.28 (d, C-4), 112.96 (s, C-5), 112.57 (d, C-9), 98.11 (d, C-7), 84.02 (d, C-2), 81.84 (s, C-1′), 64.35 (t, C-2′), 29.25 (t, C-3), 21.88, 20.71 (q, $COCH_3$), 16.08 (q, C-1″); EIMS *m*/*z* 346 [M]$^+$ (16), 213 (100), 187 (14), 43 (27); HRFABMS *m*/*z* 347.1133 (calcd for $C_{18}H_{18}O_7$ [M + H]$^+$ 347.1131).

Acetylation of 1b. Compounds **7b** and **8b** were obtained from **1b** in the same way as described above. The purification was also carried out by preparative TLC (petroleum ether−Me_2CO 3:2) giving **7b** (11.1 mg, 30%, R_f 0.23) and **8b** (14.8 mg, 35%, R_f 0.36).

Monoacetate 7b: white prisms; mp 155−156 °C; UV, IR, ^{1}H and ^{13}C NMR, EIMS and HRFABMS identical to those of dorsteniol monoacetate.

Diacetate 8b: white prisms; mp 85 °C; UV (EtOH) λ_{max} (log ϵ) 202 (4.35), 221 (3.91), 333 (3.99) nm; IR (KBr) ν_{max} 1746, 1718, 1626, 1570, 1122 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) 7.60 (1H, d, J = 9.4 Hz, H-10), 7.22 (1H, t, J = 1.2 Hz, H-4), 6.75 (1H, s, H-7), 6.23 (1H, d, J = 9.4 Hz, H-9), 5.27 (1H, t, J = 8.8 Hz, H-2), 4.54 (1H, d, J = 11.6 Hz, H-2′a), 4.50 (1H, d, J = 11.6 Hz, H-2′b), 3.28 (2H, dd, J = 8.8, 1.2 Hz, H-3), 2.02 (3H, s, $COCH_3$), 2.01 (3H, s, $COCH_3$), 1.57 (3H, s, CH_3-1″); ^{13}C NMR ($CDCl_3$, 75.4 MHz) 170.09, 170.03 (s, $COCH_3$), 162.98 (s, C-7a), 161.24 (s, C-8), 155.74 (s, C-6), 143.49 (d, C-10), 124.03 (s, C-3a), 123.14 (d, C-4), 112.85 (s, C-5), 112.53 (d, C-9), 98.10 (d, C-7), 86.05 (d, C-2), 82.03 (s, C-1′), 64.34 (t, C-2′), 29.55 (t, C-3), 21.90, 20.66 (q, $COCH_3$), 17.78 (q, C-1″); EIMS *m*/*z* 346 [M]$^+$ (15), 213 (100), 187 (15), 43 (25); HRFABMS *m*/*z* 347.1144 (calcd for $C_{18}H_{18}O_7$ [M + H]$^+$ 347.1131).

X-ray Structure Analysis of 7b.[13] X-ray data collections were carried out on a Nicolet R3m four circle diffractometer equipped with Cu Kα radiation (λ = 1.54178 Å). The diffractometer was operated in the θ:2θ scanning mode. Crystal parameters: empirical formula $C_{16}H_{16}O_6$, molecular weight 304.302, crystal system orthorhombic, space group $P2_12_12_1$, crystal size 0.70 × 0.30 × 0.04 mm, unit cell: a = 6.671 (2) Å, b = 7.727 (2) Å, c = 28.75 (1) Å, V = 1482.12 Å^3, density (calculated) = 1.36 g cm^{-3}, Z = 4. Data collection parameters: scan width below $K_{\alpha 1}$ and above $K_{\alpha 2}$, 1.0−1.2°, scan limits 3 ≤ 2θ ≤ 110, exposure time = 26.22 h. A total of 1151 reflections was collected, of which 1145 [I = 3σ(I)] were considered as observed. The data measured were corrected for background, Lorentz, and polarization effects, while crystal decay and absorption were negligible. The structure was solved by direct methods using the software provided by the diffractometer manufacturer. For the structural refinements the nonhydrogen atoms were treated anisotropically; the hydroxyl hydrogen became evident from a ΔF synthesis, and the hydrogen atoms bonded to carbons, included in the structure factor calculation, were refined isotropically. A few reflections were excluded from the final refinement calcula-

tions to improve the fit. Structure refinement: reflections for final refinement 964, parameters refined 211, $R(F)$ 4.56%, $R_w(F)$ 5.03%, goodness of fit for the last cycle 1.089, final G 0.00184, residual electron density 0.20 eÅ^{-3}.

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(13) Crystallographic data for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre. Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-(0)1223−336033 or E-mail: deposit@ccdc.cam.ac.uk).

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