Mammea Coumarins from the Flowers of *Mammea siamensis*

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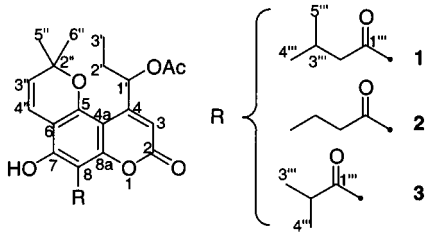
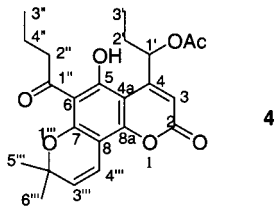
Four new mammea coumarins, mammea E/BA cyclo D (**1**), mammea E/BC cyclo D (**2**), mammea E/BD cyclo D (**3**), and mammea E/AC cyclo D (**4**), were isolated from the flowers of *Mammea siamensis*, along with six known coumarins. Extensive 1D and 2D NMR experiments and other spectroscopic studies, as well as chemical transformations, were employed to determine the structures of **1**−**4**.

Mammea siamensis (Miq.) T. Anders. is a Thai medicinal plant in the family Guttiferae, locally known as "Sa rapi" and used as a heart tonic. Plants of the genus mammea are known to be rich sources of various coumarins[1−8] and xanthones.[9,10] In 1981, the initial isolation of 4-phenylcoumarins was reported from petroleum extracts of flowers of *M. siamensis*.[5] Coumarins are reported to exhibit diverse biological activities, and their occurrence in the plant kingdom is widespread.[11]

In a continuation of our study on the flowers of this plant,[7] we now report the isolation and structure elucidation of four new mammea coumarins (**1**−**4**). The structures of these new coumarins were determined using 1D and 2D NMR techniques (^{1}H, ^{13}C NMR, COSY, HETCOR or HMQC, and COLOC or HMBC).





Ten compounds were isolated from fraction E-2 of a hexane extract of the flowers of *M. siamensis* by successive silica gel column chromatography, preparative TLC, and HPLC. Four new compounds, mammea E/BA cyclo D (**1**), mammea E/BC cyclo D (**2**), mammea E/BD cyclo D (**3**), and mammea E/AC cyclo D (**4**), were identified by means of spectroscopic studies and confirmed by chemical transformations. Six known coumarins, mammea A/BC,[12] mammea B/AC cyclo D,[4,7] mammea A/AC cyclo D,[5−7] mammea B/AC cyclo F,[3,8,13] mammea A/AA cyclo F,[1,3,4,8] and mammea A/AC cyclo F,[3,8,9] were also isolated and established by comparison of their spectral data with those described in the literature.

Coumarin **1** was isolated as a yellow semisolid, which was shown to be optically active ($[\alpha]^{26}_D$ −68.8°, *c* 0.07). The compound gave a parent ion by HRFABMS (negative ion) at *m/z* 427.1753 $[M - H]^-$, corresponding to a molecular formula $C_{24}H_{28}O_7$. The EIMS showed the molecular ion at *m/z* 428 and fragment ions at *m/z* 413 $([M - CH_3])^+$, 385, 371, and 353. Its IR spectrum showed absorption bands corresponding to the carbonyl groups of an ester and an aryl ketone at 1732 and 1645 cm^{-1}, respectively. The NMR spectrum (Table 1) revealed signals at δ 6.60 (1H, dd, J = 8.8, 2.8 Hz), 1.99 (1H, ddq, J = 14.5, 7.3, 2.8 Hz), 1.67 (1H, ddq, J = 14.5, 7.3, 8.8 Hz), 1.05 (3H, t, J = 7.3 Hz), and 2.18 (3H, s), which are due to the presence of a 1-acetoxypropyl group. The signal at δ 14.54 (1H, s) was ascribed to a phenolic group hydrogen bonded to an acyl group. Two singlets of three hydrogens each at δ 1.56 and 1.59 and the presence of two doublets of one hydrogen each at δ 5.61 (J = 10.0 Hz) and 6.74 (J = 10.0 Hz) established the presence of a 2,2-dimethyl-Δ^3-pyran ring.[5] Substitution at C-4 of the coumarin nucleus was apparent from the C-3 proton singlet at δ 6.30 (1H). The nature of the substituent at C-8 was deduced to be a 3-methylbutyryl chain from the doublet of doublets of one hydrogen each at δ 3.12 and 3.15 with coupling constants of 15.5 and 6.6 Hz, a multiplet of one proton at δ 2.27, and two doublets of three hydrogens each at δ 1.03 and 1.026 with a coupling constant of 6.7 Hz. From the proton-decoupled ^{13}C NMR spectrum of **1** (Table 2), 24 signals were observed. The DEPT spectra (DEPT 90 and 135) of **1** exhibited six methyl carbon atoms at δ 10.0 (C-3′), 28.5 (C-5″), 27.8 (C-6″), 22.6 (C-4‴ and C-5‴), and 21.0 (methyl carbon atom of acetoxyl group), two methylene carbon atoms at δ 53.6 (C-2‴) and 28.7 (C-2′), three olefinic methine carbon atoms at δ 106.6 (C-3), 126.8 (C-3″), and 115.8 (C-4″), two methine carbon atoms at δ 25.5 (C-3‴) and 73.0 (C-1′), and 11 quaternary carbon atoms at δ 159.2 (C-2), 157.3 (C-4), 100.9 (C-4a), 155.8 (C-5), 106.5 (C-6), 163.3 (C-7), 104.7 (C-8), 157.1 (C-8a), 170.3 ($OCOCH_3$), 80.3 (C-2″), and 206.2 (C-1‴).

The position of the phenolic group at C-7 in **1** was established by the COLOC NMR spectral data (Figure 1) of the phenolic proton O*H*-7 to C-7, C-6, and C-8 as well as the NOE interaction with H-4″, thereby locating the pyran ring of **1** between C-5 and C-6. Additionally, the proton signal of H-3 at δ 6.30 showed a cross-peak with the carbon signals of C-2, C-4a, and C-1′, and a cross-peak

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Table 1. ^{1}H NMR Spectral Data of Compounds **1**−**3** in $CDCl_3$ (400 MHz, *J* in Hz)

position	1	2	3
3	6.30, s	6.30, s	6.31, s
O*H*-7	14.54, s	14.51, s	14.44, s
1′	6.60, dd (8.8, 2.8)	6.59, dd (8.9, 2.9)	6.61, dd (8.8, 2.7)
COO*CH*$_3$	2.18, s	2.18, s	2.18, s
2′a	1.99, ddq (14.5, 7.3, 2.8)	1.99, ddq (14.5, 7.1, 2.9)	2.00, ddq (14.5, 7.4, 2.7)
2′b	1.67, ddq (14.5, 7.3, 8.8)	1.65, ddq (14.5, 7.1, 8.9)	1.66, ddq (14.5, 7.4, 8.8)
3′	1.05, t (7.3)	1.06, t (7.1)	1.06, t (7.4)
chromene moiety			
3″	5.61, d (10.0)	5.61, d (10.0)	5.61, d (10.0)
4″	6.74, d (10.0)	6.73, d (10.0)	6.74, d (10.0)
5″	1.56, s	1.56, s	1.57, s
6″	1.59, s	1.59, s	1.60, s
8-acyl moiety			
2‴	3.12, dd (15.5, 6.6) 3.15, dd (15.5, 6.6)	3.26, t (7.3)	4.03, septet (6.7)
3‴	2.27, m	1.78, sextet (7.3)	1.27, d (6.7)
4‴	1.03, d (6.7)	1.03, t (7.3)	1.27, d (6.7)
5‴	1.026, d (6.7)		

Table 2. ^{13}C NMR Spectral Data of Compounds **1**−**3** in $CDCl_3$ (100 MHz)[a]

carbon	1	2	3
2	159.2 (s)	159.3 (s)	159.3 (s)
3	106.6 (d)	106.5 (d)	106.5 (d)
4	157.3 (s)	157.4 (s)	155.5 (s)
4a	100.9 (s)	100.9 (s)	101.7 (s)
5	155.8 (s)	156.0 (s)	155.7 (s)
6	106.5 (s)	106.5 (s)	106.6 (s)
7	163.3 (s)	163.2 (s)	163.5 (s)
8	104.7 (s)	104.5 (s)	103.8 (s)
8a	157.1 (s)	157.1 (s)	156.8 (s)
1′	73.0 (d)	73.1 (d)	73.0 (d)
O*C*OCH$_3$	170.3 (s)	170.3 (s)	170.3 (s)
OCO*C*H$_3$	21.0 (q)	21.0 (q)	20.2 (q)
2′	28.7 (t)	28.7 (t)	28.7 (t)
3′	10.0 (q)	10.0 (q)	10.0 (q)
chromene moiety			
2″	80.3 (s)	80.3 (s)	80.2 (s)
3″	126.8 (d)	126.8 (d)	126.8 (d)
4″	115.8 (d)	115.8 (d)	115.9 (d)
5″	28.5 (q)	28.5 (q)	28.4 (q)
6″	27.8 (q)	27.8 (q)	27.8 (q)
8-acyl moiety			
1‴	206.2 (s)	206.4 (s)	210.8 (s)
2‴	53.6 (t)	46.7 (t)	40.4 (d)
3‴	25.5 (d)	18.0 (t)	19.2 (q)
4‴	22.6 (q)	13.8 (q)	19.2 (q)
5‴	22.6 (q)		

[a] Multiplicities were determined by the DEPT pulse sequence.

of the H-1′ signal at δ 6.60 with the C-4 carbon signal was also observed. These results clearly indicated that the 1-acetoxypropyl substituent was attached to C-4. The bathochromic shift (372 nm to 390 nm) with alkali of its UV spectrum suggested that **1** contains an 8-acylcoumarin chromophore.[2,13] On the basis of the above evidence, therefore, compound **1** was characterized as mammea E/BA cyclo D.

Coumarin **2** was isolated as a yellow solid and recrystallized from a mixture of dichloromethane−hexane as yellow needles. Compound **2** has a molecular formula of $C_{23}H_{26}O_7$ determined from its positive-ion HRFABMS. The UV (λ_{max} 269, 305, 373; in base 208, 250, 391 nm), IR (ν_{max} 1732, 1644 cm^{-1}), and ^{1}H (Table 1) and ^{13}C NMR (Table 2) spectra of **2** were almost identical with those of compound **1**. However, coumarin **2** showed different ^{1}H and ^{13}C NMR spectral data from those of **1** only in the signals of the 8-acyl group. In compound **2**, proton signals appeared at δ 3.26 (2H, t, J = 7.3 Hz), 1.78 (2H, sextet, J = 7.3 Hz), and 1.03 (3H, t, J = 7.3 Hz) and carbon signals at δ 206.3 (C-1‴), 46.7 (C-2‴), 18.0 (C-3‴), and 13.8 (C-4‴) due to the presence of a butyryl group. The positions of the butyryl group and the pyran ring in **2** were confirmed by acetylation, which resulted in the appropriate NMR upfield shift of 0.42 ppm of H-4″ in the chromene ring. The diamagnetic shift of the H-4″ resonance required its placement peri to the OAc-7 group, thereby locating the pyran ring between C-5 and C-6 in **2**.[14] The COLOC spectrum (Figure 1) revealed three- and two-bond correlations between the O*H*-7 proton with C-6, C-7, and C-8. On the basis of the above evidence, therefore, compound **2** was assigned as mammea E/BC cyclo D.

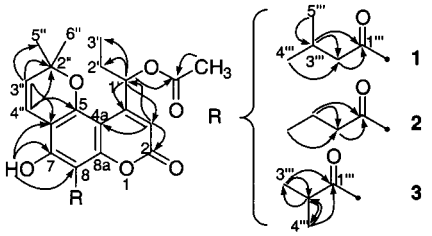
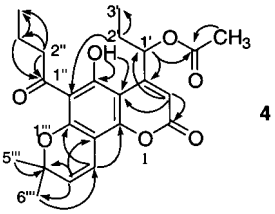


Figure 1. COLOC correlations for **1** and **2** and HMBC correlations for **3**.

Compound **3** was recrystallized from dichloromethane as yellow crystals. The UV, IR, HRFABMS, and EIMS data for compound **3** closely resembled those for compound **2**. The ^{1}H (Table 1) and ^{13}C NMR (Table 2) spectra of **3** were almost identical with those of compounds **1** and **2**. However, compound **3** showed ^{1}H and ^{13}C NMR spectral data that were different from those of **1** and **2** only in the signal of the 8-acyl group. Compound **3**, which has a 2-methylpropionyl group, showed proton signals at δ 4.03 (septet, J = 6.7 Hz, H-2‴) and 1.27 (d, J = 6.7 Hz, H-3‴ and H-4‴) and carbon signals at δ 210.8 (C-1‴), 40.4 (C-2‴), and 19.2 (C-3‴ and C-4‴). The HMBC (Figure 1) and UV spectra supported the position of the acyl substituent in compound **3** at C-8. On the basis of the above evidence, therefore, compound **3** was characterized as mammea E/BD cyclo D.

Compound **4** was isolated as a yellow gum which was shown to be optically active ($[\alpha]^{31}_D$ +8°, *c* 0.12). The IR spectrum of **4** showed a band that was ascribed to an α,β-unsaturated δ-lactone (1729 cm^{-1}) group. The molecular formula of **4** was determined to be $C_{23}H_{26}O_7$ from the positive-ion HRFABMS (calcd *m*/*z* 415.1757 for $C_{23}H_{27}O_7$, found 415.1755). In addition, the EIMS of **4** showed a fragmentation pattern similar to those of compounds **2** and **3**. Extensive NMR analysis of **4** showed that this coumarin has the same substituents as **2** since an 1-acetoxypropyl,



4

Figure 2. HMBC correlations for compound **4**.

a butyryl, and a 2,2-dimethyl Δ^3 pyran ring were revealed from its ^{1}H and ^{13}C NMR spectral data. However, **2** and **4** exhibited quite different shifts with alkaline reagents in their UV spectral data. It was therefore deduced that **4** is a regioisomer of compound **2**.

The HMBC spectral data of **4** (Figure 2) revealed three- and two-bond correlations between the O*H*-5 proton with the C-4a (101.5), C-5 (164.4), and C-6 (107.1) signals, and the UV spectral data supported the position of the acyl substituent in compound **4** at C-6.[2,13] The angular fusion of the pyran ring was confirmed by acetylation of **4** to the corresponding acetate derivative. The ^{1}H NMR of the acetate derivative of **4** showed downfield shifts of 0.14 ppm for H-3‴ and 0.06 ppm for H-4‴ in the chromene ring.[14] On the basis of the above evidence, therefore, compound **4** was characterized as mammea E/AC cyclo D.

Experimental Section

General Experimental Procedures. Melting points were determined on an electrothermal melting point apparatus (Electrothermal 9100) and are reported without correction. Optical rotations were measured in chloroform solution at the sodium D line (589 nm) on a JASCO DIP-370 digital polarimeter. UV spectra were measured with Shimadzu UV−vis 2001S spectrophotometer. Infrared spectra were obtained from Perkin-Elmer System 2000 FT-IR or JASCO A-302 spectrometers. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM 400 and a Varian Gemini 2000; $CDCl_3$ was used as the solvent and TMS as an internal standard. Chemical shifts are given in parts per million downfield from TMS, and coupling constants are measured in Hz. DEPT, HETCOR/HMQC, COSY, COLOC/HMBC, NOE, and COSY NMR experiments were obtained using standard Bruker software. Mass spectra were determined using GC−MS Finnigan INCOS 50 and GC−MS MAT 90 instruments. HPLC was performed on a Thermo Separation Products system (San Jose, CA) (pump, P4000; detecter, UV6000LP for analysis, UV2000 for preparative). The HPLC conditions were as follows: (a) LUNA 5 μm C_8 stainless steel column, 150 × 4.60 mm, cat. no. 00F-4040-E0 for analytical applications; (b) LUNA 10 μm C_8 100 A stainless steel column, 250 × 21.20 mm, cat. no. 00G-4093-P0 for preparative applications. Compounds were purified by isocratic separation using H_2O−MeOH as mobile phase; scanning wavelengths were from 190 to 420 nm. Column chromatography was carried out using Si gel 60 (0.063−0.200 mm) and Si gel 60 (particle size less than 0.063 mm). TLC and preparative TLC were carried out on Si gel 60 F_{254} plates (cat. no. 7747 E. Merck). Compounds were detected by their UV absorbance at 254 and 366 nm. All commercial grade solvents were distilled prior to use, and spectral grade solvents were used for spectroscopic measurements.

Plant Material. Dried flowers of *Mammea siamensis* were purchased from a local traditional drug store in Bangkok, in October 1995. The plant materials were further identified by Dr. Wongsatit Chuakul, Department of Pharmaceutical Botany, Faculty of Pharmacy, Mahidol University, Bangkok, Thailand. A voucher specimen (PBM3231) is deposited in the Faculty of Pharmacy, Mahidol University, Bangkok, Thailand.

Extraction and Isolation. The dried flowers (8.5 kg) of *Mammea siamensis* were extracted exhaustively with hexane at room temperature, followed by filtration. The filtrates were combined and evaporated under reduced pressure to afford a dark brown gum (428 g). The dried extract (300 g) was submitted to Si gel column chromatography and eluted with a gradient of hexane−EtOAc (0%−100%) to afford six fractions (A−F). A portion of fraction E (131 g) was then separated by column chromatography over Si gel with mixtures of EtOAc in hexane of increasing polarity to give eight fractions (E-1−E-8). Fraction E-2 was further separated by column chromatography on a Si gel column with a hexane−EtOAc gradient and produced eight further fractions (f-1−f-8). Fraction f-3 was subjected to column chromatography on Si gel with hexane−EtOAc (7%) and further purified by preparative TLC with hexane−EtOAc (7%) as developing solvent (five developments), affording 41.9 mg of **1** (R_f 0.39), 53.2 mg of **2** (R_f 0.36), 23.7 mg of **3** (R_f 0.33), 20.8 mg of mammea B/AC cyclo D (R_f 0.49), and 27.9 mg of mammea A/AC cyclo D (R_f 0.43). Fraction f-4 was subjected to column chromatography on Si gel with hexane−EtOAc (15%) and further purified by preparative TLC with hexane−EtOAc (18%; three developments) to afford 13.5 mg of mammea B/AC (R_f 0.49). Fraction f-5 was chromatographed on a Si gel column with hexane−EtOAc (20−25%) and then purified by preparative reversed-phase HPLC, run isocratically using 83.5% MeOH−H_2O with UV detection at 280 nm, with a flow rate of 8 mL/min, affording 6.6 mg of mammea B/AC cyclo F (t_R 22.18 min), 7.9 mg of mammea A/AA cyclo F (t_R 20.73 min), and 12.4 mg of mammea A/AC cyclo F (t_R 17.79 min). Fraction f-6 was chromatographed on a Si gel column with a gradient of hexane−EtOAc (25−30%) and then purified by preparative reversed-phase HPLC run isocratically using 85% MeOH−H_2O with UV detection at λ 280 nm, flow rate 8 mL/min, to afford 4.9 mg of **4**, t_R 22.56 min.

Mammea E/BA cyclo D (1): yellow semisolid; $[\alpha]^{26}_D$ −68.8° (*c* 0.07, $CHCl_3$); UV λ_{max} EtOH (log ϵ) 270 (4.29), 307 (4.17), 372 (3.73), and λ_{max} EtOH + 0.01 N NaOH (log ϵ) 209 (4.90), 250 (4.17), 390 (4.21) nm; IR ($CHCl_3$) ν_{max} 3027, 2965, 2874, 1732, 1645, 1610, 1584, 1464, 1397, 1291, 1238, 1194, 1129, 1045, 971, 884, 668 cm^{-1}; ^{1}H NMR and ^{13}C NMR, see Tables 1 and 2, respectively; EIMS *m/z* 428 $[M]^+$ (40), 413 $[M - CH_3]^+$ (100), 385 (27), 371 (51), 353 (35), 300 (53); HRFABMS (negative ion) *m/z* 427.1753 (calcd for $C_{24}H_{27}O_7$, 427.1757).

Mammea E/BC cyclo D (2): yellow needles; mp 139−140 °C; $[\alpha]^{26}_D$ −48.6° (*c* 0.205, $CHCl_3$); UV λ_{max} EtOH (log ϵ) 269 (4.39), 305 (4.43), 373 (4.02), and λ_{max} EtOH + 0.01 N NaOH (log ϵ) 208 (5.32), 250 (sh), 391 (4.48) nm; IR ($CHCl_3$) ν_{max} 3026, 2974, 1732, 1644, 1610, 1584, 1463, 1396, 1209, 1193, 1151, 1122, 1101, 1045, 970, 884 cm^{-1}; ^{1}H NMR and ^{13}C NMR, see Tables 1 and 2, respectively; EIMS *m/z* 414 $[M]^+$ (47), 399 $[M - CH_3]^+$ (100), 371 (33), 357 (48), 339 (20); HRFABMS (positive ion) *m/z* 415.1762 (calcd for $C_{23}H_{27}O_7$, 415.1757).

Acetylation of 2. Treatment of compound **2** (10 mg) with acetic anhydride (1 mL), 4-*N*,*N*-(dimethylamino)pyridine (0.5 mg), and pyridine (1 mL) at room temperature for 2 h gave the acetate derivative of **2** (9.5 mg, 86%): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 6.40 (1H, s, H-3), 2.32 (3H, s, OCO*CH*$_3$-7), 6.58 (1H, dd, J = 8.5, 3.0 Hz, H-1′), 2.19 (3H, s, OCO*CH*$_3$-1′), 2.0 (1H, m, H-2′a), 1.66 (1H, m, H-2′b), 0.98 (3H, t, J = 7.2 Hz, H-3′), 5.72 (1H, d, J = 10.0 Hz, H-3″), 6.31 (1H, d, J = 10.0 Hz, H-4″), 1.59 (3H, s, H-5″), 1.56 (3H, s, H-6″), 2.94 (2H, t, J = 7.2 Hz, H-2‴), 1.70 (2H, m, H-3‴), 1.05 (2H, t, J = 7.1 Hz, H-4‴).

Mammea E/BD cyclo D (3): yellow crystals; mp 82−83 °C; $[\alpha]^{31}_D$ −24.2° (*c* 0.16, $CHCl_3$); UV λ_{max} EtOH (log ϵ) 269 (4.29), 305 (4.24), 385 (3.97), and λ_{max} EtOH + 0.01 N NaOH (log ϵ) 207 (5.28), 250 (sh), 390 (4.28) nm; IR ($CHCl_3$) ν_{max} 2929, 1733, 1608, 1386, 1230, 1144 cm^{-1}; ^{1}H NMR and ^{13}C NMR, see Tables 1 and 2, respectively; EIMS *m/z* 414 $[M]^+$ (25), 399 $[M - CH_3]^+$ (100), 371 $[M - CH_3CO]^+$ (20), 357 (49), 339 (27); HRFABMS (positive ion) *m/z* 415.1751 (calcd for $C_{23}H_{27}O_7$, 415.1757).

Mammea E/AC cyclo D (4): yellow gum; $[\alpha]^{31}_D$ +8° (*c* 0.12, $CHCl_3$); UV λ_{max} EtOH (log ϵ) 226 (4.19), 285 (4.35), and λ_{max} EtOH + 0.01 N NaOH (log ϵ) 209 (5.19), 309 (4.29), 422 (3.88) nm; IR ($CHCl_3$) ν_{max} 2929, 2857, 1729, 1608, 1477, 1391, 1230, 1123 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.20 (1H, br s, H-3),

15.60 (1H, s, OH-5), 6.53 (1H, dd, J = 8.4, 2.6 Hz, H-1′), 2.16 (3H, s, COOCH_3), 2.01 (1H, ddq, J = 14.4, 7.3, 2.6 Hz, H-2′), 1.65 (1H, ddq, J = 14.4, 7.3, 8.4 Hz, H-2′), 1.04 (3H, t, J = 7.3 Hz, H-3′), 3.09 (2H, br t, J = 7.4 Hz, H-2″), 1.75 (2H, sextet, J = 7.4 Hz, H-3″), 1.03 (3H, t, J = 7.4 Hz, H-4″), 5.61 (1H, d, J = 10.0 Hz, H-3‴), 6.82 (1H, d, J = 10.0 Hz, H-4‴), 1.56 (3H, s, H-5‴), 1.55 (3H, s, H-6‴); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.0 (s, C-2), 106.3 (d, C-3), 158.0 (s, C-4), 101.5 (s, C-4a), 164.4 (s, C-5), 107.1 (s, C-6), 158.0 (s, C-7), 101.8 (s, C-8), 154.6 (s, C-8a), 73.8 (d, C-1′), 170.3 (s, OCOCH$_3$), 21.0 (q, OCOCH_3), 28.6 (t, C-2′), 10.3 (q, C-3′), 207.5 (s, C-1″), 46.8 (t, C-2″), 18.2 (t, C-3″), 13.9 (q, C-4″), 79.9 (s, C-2‴), 126.5 (d, C-3‴), 115.5 (d, C-4‴), 208.3 (q, C-5‴), 28.2 (q, C-6‴); EIMS m/z 414 $[M]^+$ (29), 399 $[M - CH_3]^+$ (100), 371 $[M - CH_3CO]^+$ (20), 357 (49), 339 (27); HRFABMS (positive ion) m/z 415.1755 (calcd for $C_{23}H_{27}O_7$, 415.1757).

Acetylation of Compound 4. Compound **4** (4.9 mg) was dissolved in 0.5 mL of pyridine and 1 mL of Ac_2O using *N*,*N*-(dimethylamino)pyridine as a catalyst. The reaction mixture was stirred at room temperature for 2 h. After the usual workup, the product was isolated by preparative TLC using 18% ethyl acetate in hexane to give the acetate derivative of **4** (2.8 mg, 52%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.41 (1H, s, H-3), 2.33 (3H, s, OCOCH_3-5), 6.23 (1H, br d, J = 5.71 Hz, H-1′), 2.16 (3H, s, OCOCH_3-1′), 1.95 (1H, m, H-2′a), 1.66 (1H, m, H-2′b), 0.98 (6H, t, J = 7.3 Hz, H-3′ and H-4″), 2.83 (1H, t, J = 7.3 Hz, H-2″a), 2.82 (1H, t, J = 7.3 Hz, H-2″b), 1.70 (2H, m, H-3″), 5.75 (1H, d, J = 10.0 Hz, H-3‴), 6.88 (1H, d, J = 10.0 Hz, H-4‴), 1.51 (1H, s, H-5‴), 1.52 (3H, s, H-6‴).

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