Cytotoxic Prenylflavonoids from *Artocarpus elasticus*

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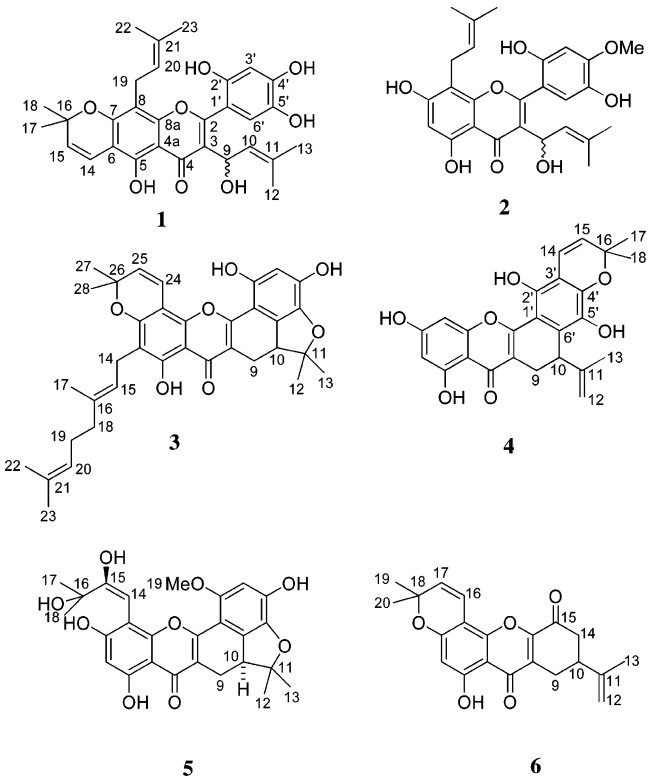
Five new prenylated flavonoids, artelastoheterol (**1**), artelasticinol (**2**), cycloartelastoxanthone (**3**), artelastoxanthone (**4**), and cycloartelastoxanthendiol (**5**), along with five known compounds, were isolated from the root bark of *Artocarpus elasticus*. The structures of **1**−**5** were elucidated by spectroscopic methods and through comparison with data reported in the literature. The previously known compound artonol A (**6**) exhibited cytotoxic activity against the A549 human cancer cell line, with an ED_{50} value of 1.1 μg/mL.

Wood and bark from *Artocarpus* species, a Southeast Asian genus of about 50 arboreal species, are rich in prenylated flavonoids.[1] Prenylflavonoids isolated from *Artocarpus communis* and *A. elasticus* revealed significant cytotoxic effect against human cancer cell lines.[2,3] To study the structure−cytotoxic activity relationships of various prenylflavonoids isolated from *Artocarpus* species, we have investigated the constituents of the root bark of Formosan *A. elasticus* and isolated five new prenylflavonoids, artelastoheterol (**1**), artelasticinol (**2**), cycloartelastoxanthone (**3**), artelastoxanthone (**4**), and cycloartelastoxanthendiol (**5**), along with five known compounds, artonin F, artonols A (**6**) and B, cycloartobiloxanthone, and cyclomorusin. In the present paper, the structure elucidation of **1**−**5** and the cytotoxic activity of these additional constituents of *A. elasticus* are reported.



Artelastoheterol (**1**) was obtained as an orange gum, and the molecular formula was determined to be $C_{30}H_{32}O_8$ from its HREIMS and NMR data. The IR spectrum showed absorption bands for hydroxyl (3395 cm^{-1}), conjugated carbonyl (1652 cm^{-1}), and aromatic ring (1620 cm^{-1}) functionalities. The UV spectrum was similar to that of heterophyllin.[4] The ^{13}C NMR spectrum revealed the presence of 30 signals, including those for a carbonyl group (δ 178.8), a quaternary carbon (δ 77.7), and six methyl groups, corresponding to a diprenylated flavone with a 2,2-dimethylpyran ring. The ^1H NMR spectrum indicated signals for a chelated phenolic proton [δ 12.80 (1H, s)], a 2,2-dimethylpyran ring [δ 6.69 (1H, d, J = 10.0 Hz), 5.59 (1H, d, J = 10.0 Hz), and 1.44 and 1.45 (each 3H, s)], a 3,3-dimethylallyl group [δ 5.22 (1H, t, J = 6.4 Hz), 3.45 (2H, m), 1.66 (3H, s), and 1.81 (3H, s)], two tertiary methyl groups that appeared to have four slightly different chemical shifts [δ 1.922 and 1.919, 1.664 and 1.661], an oxymethine proton [δ 6.18 (1H, bd, J = 9.2 Hz)], an olefinic proton [δ 5.44 (1H, m)] on a 1-hydroxy-3,3-dimethylallyl group,[5] and two aromatic protons [δ 6.45 (s) and 7.25 (s)]. Its optical inactivity indicated that **1** was isolated as a racemic mixture.[6,7] In the ^{13}C NMR spectrum of **1** (Table 1), the chemical shifts were very similar to the corresponding data of cycloheterophyllin,[4] except for those of C-2 to C-4, C-11, C-1′, C-2′, and C-5′. The HMBC correlations for H-9/C-2, C-3, C-4, C-10, and C-11, H-10/Me-12 and Me-13, Me-12/C-13, and Me-13/C-12 confirmed that the 1-hydroxy-3,3-dimethylallyl group is located at C-3 in **1**. The HMBC correlations for H-14/C-5 and C-7 and for H-15/C-6 substantiated that the 2,2-dimethyl-6*H*-pyran group is located at C-6 and C-7. In turn, the HMBC correlations for H_2-19/C-7, C-8, and C-8a established that the prenyl group is located at C-8. The proton and carbon signals of **1** (Table 1 and Experimental Section) were assigned fully by 1D and 2D NMR methods and by comparison with data reported in the literature.[4,8] The EIMS showed fragment peaks at *m/z* 518 $[M - 2]^+$,[9] 502 $[M - H_2O]^+$, 447 $[M - H_2O - C_4H_7]^+$, and 391 $[M - H_2O - (C_4H_7)_2 - H]^+$ and supported the structure of **1**. In addition to the above evidence, the HMBC correlations between at H-3′/C-1′, C-2′, C-4′, and C-5′ and H-6′/C-2′ were used to establish the structure of artelastoheterol (**1**) as 5,2′,4′,5′-tetrahydroxy-6,7-(2,2-dimethyl-6*H*-pyrano)-8-prenyl-3-(9-hydroxy)prenyl-flavone (**1**).

Artelasticinol (**2**), an orange gum, was assigned a molecular formula of $C_{26}H_{28}O_7$ from its HREIMS and NMR

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Table 1. ^{13}C NMR Spectroscopic Data of **1**−**5** (100 MHz, δ in ppm)

position	**1**[a]	**2**[a]	**3**[b]	**4**[a]	**5**[c]
2	151.5	158.1	162.0	161.9	161.6
3	109.7	109.8	112.8	112.7	103.6
4	178.8	178.8	182.1	181.6	180.8
4a	105.3	105.5	105.4	105.6	104.7
5	154.4	154.0	160.2	163.8	160.2
6	105.2	99.8	112.7	100.4	103.6
7	156.5	164.5	158.0	165.1	162.3
8	107.6	109.5	101.9	95.6	104.1
8a	153.6	160.1	158.0	158.1	155.4
1′	107.9	108.7	105.6	107.8	112.2
2′	155.4	155.3	152.2	146.1	151.9
3′	104.8	102.2	106.0	111.1	105.6
4′	149.7	160.3	147.6	146.0	148.7
5′	138.9	109.1	138.5	137.9	138.1
6′	109.3	139.3	134.3	129.2	132.2
9	69.3	69.9	21.0	22.8	20.4
10	121.0	121.0	48.2	38.4	47.9
11	139.1	134.6	94.3	145.9	93.1
12	25.9	25.9	23.5	112.5	22.7
13	18.6	18.6	28.9	22.6	26.4
14	115.9	21.8	22.5	117.9	34.8
15	127.9	124.9	123.9	130.4	67.8
16	77.7	134.7	123.1	78.9	76.5
17	28.1	25.7	28.0	28.7	28.7
18	28.2	18.0	43.0	28.7	28.1
19	21.5	55.6	24.2		54.2
20	122.1		125.5		
21	131.7		132.7		
22	25.7		26.4		
23	18.1		18.7		
24			117.5		
25			126.9		
26			81.8		
27			27.9		
28			27.9		

[a] In $CDCl_3$. [b] In acetone-d_6. [c] In pyridine-d_5.

data. The ^1H NMR spectrum revealed signals for a chelated hydroxyl group [δ 12.78 (1H, brs)], a 1-hydroxy-3,3-dimethylallyl group[5] [δ 6.27 (1H, bd, J = 9.2 Hz), 5.45 (1H, m), and two tertiary methyl groups appeared to have four slightly different chemical shifts (δ 1.982, 1.978, 1.709, and 1.705)], a 3,3-dimethylallyl group [δ 5.30 (1H, t, J = 6.4 Hz), 3.57 (1H, d, J = 6.4 Hz), and 1.87, 1.76 (each 3H, s)], and a set of aromatic protons in an ABX system [δ 7.66 (1H, d, J = 8.8 Hz), 6.61 (1H, dd, J = 8.8, 2.4 Hz), and 6.48 (1H, d, J = 2.4 Hz)]. It also exhibited a methoxy signal at δ 3.84 and a singlet aromatic proton at δ 6.32. By comparing the NMR spectra of **2** with those of **1**, it became clear that **2** lacks a 2,2-dimethylpyran ring in the A ring. The optical inactivity of **2** showed that **2** is also a racemic mixture.[6,7] The H_2-14 and H-6 signals of **2** were observed in the same region as those of other 8-prenylflavonoids,[10] and the UV spectrum indicated a bathocromic shift upon addition of $AlCl_3$.[11] Thus, the above result confirmed that the prenyl group is located at C-8 in **2**. The UV spectrum of **2** exhibited absorption maxima [λ_{max} 215, 273, 295 (sh), 370 nm] suggestive of a 8-prenyl-5,7,2′,4′-tetraoxygenated flavone derivative.[4,12] The absence of bathochromic shifts upon the addition of NaOMe and the NOESY correlation between MeO-4′/H-3′ and H-5′ suggested that the methoxy group is located at C-4′ in **2**. Thus, artelasticinol (**2**) was elucidated as 5,7,2′5′-tetrahydroxy-4′-methoxy-8-prenyl-3-(9-hydroxy)prenylflavone. The ^{13}C NMR spectrum (Table 1) was assigned by 1D and 2D NMR techniques and comparison with the data of **1** and reported data in the literature for structurally related compounds.[5] The ^{13}C NMR data and EIMS also supported the structure of **2**.

Cycloartelastoxanthone (**3**), also an orange gum, exhibited a molecular formula of $C_{35}H_{38}O_7$, as determined on the basis of its HREIMS and NMR data. Its IR and UV spectra were similar to those of artonin F.[13] This suggested that **3** possesses a 5,2′,4′-trihydroxy flavone moiety. The ^1H NMR spectrum of **3** showed signals for three hydroxyl groups [δ 13.70 (1H, s), 9.17 (1H, brs), and 8.94 (1H, brs)], a 2,2-dimethylpyran ring [δ 6.99 (1H, d, J = 10.0 Hz), 5.63 (1H, d, J = 10.0 Hz), and 1.42 (6H, s)], a geranyl group [δ 5.23 (1H, t, J = 7.2 Hz), 5.12 (1H, m), 3.31 (2H, d, J = 7.2 Hz), 2.13 (2H, m), 1.79 (3H, s), 1.73 (2H, m), 1.63 and 1.44 (each 3H, s)], an ABX system [δ 3.39 (1H, dd, J = 15.2, 7.2 Hz), 3.20 (1H, dd, J = 15.2, 7.2 Hz), and 2.34 (1H, t, J = 15.2 Hz)], and two tertiary methyl groups [δ 1.64 and 1.31 (each 3H, s)]. In the ^{13}C NMR spectrum of **3** (Table 1), the chemical shift values were almost identical to those of artonin F,[13] except for C-14 to C-23. In an HMBC experiment on **3**, the proton signal at δ 3.31 (H_2-14) was correlated with C-7, C-6, and C-5, which suggested that the geranyl side chain is located at C-6. The EIMS showed significant peaks at m/z 555 $[M - Me]^+$, 515 $[M - a]^+$, and 487 $[M - b]^+$ (Figure S1, Supporting Information), which further supported the structure of **3**. A combination of 2D NMR techniques, inclusive of $^1H-^1H$ COSY, HMQC, HMBC, and NOESY experiments, enabled the assignments of the ^1H and ^{13}C NMR data for **3** (Table 1 and Experimental Section). Consequently, the structure of cycloartelastoxanthone (**3**) was determined as 9-geranyl-5,5a,6,11-tetrahydro-1,3,8-trihydroxy-5,5,11,11-tetramethylbenzofuro-[3,3*a*,4:*ab*]pyrano[2′,3′:*j*]xanthen-7-one.

Artelastoxanthone (**4**), obtained as an orange gum, was assigned a molecular formula of $C_{25}H_{22}O_7$ on the basis of its HRESIMS and NMR data. In the ^1H NMR spectrum, the chemical shift values and coupling patterns of all proton signals except those of two meta-coupled aromatic protons [δ 6.28 (d, J = 2.4 Hz) and 6.58 (d, J = 2.4 Hz)] were similar to those of the relevant protons of artonol E.[14] Similarly, in the ^{13}C NMR spectrum of **4**, the chemical shift values of all the carbon signals except the signals for C-5 to C-8, C-4a, and C-8a were similar to those of the corresponding carbon signals of artonol E.[14] On the basis of the above result and analysis of its HMQC, HMBC, and NOESY spectra, the structure of artelastoxanthone (**4**) was characterized as 5,6-dihydro-1,4,8,10-tetrahydroxy-5-(1-methylethenyl)-7*H*-3,2-(2′,2′-dimethylchromeno)[*a*]xanthen-7-one.

As a result of the work carried out in this investigation, it was not possible to establish the correct relative configuration for the C-9 hydroxy group in compounds **1** and **2** or for the C-10 isopropenyl group in compound **4**.

The molecular formula of cycloartelastoxanthendiol (**5**) was determined to be $C_{26}H_{28}O_9$ from its HRESIMS (m/z 467.1708 $[M - H_2O + H]^+$), which is consistent with its ^1H and ^{13}C NMR data. The IR spectrum showed hydroxyl (3395 cm^{-1}) and conjugated carbonyl (1652 cm^{-1}) bands. The UV spectrum and the appearance of two proton signals at δ 1.35 and 1.68 (3H, s, each) and an ABX system of proton signals at δ 2.44 (1H, t, J = 15.2 Hz), 3.43 (1H, dd, J = 15.2, 7.2 Hz), and 3.23 (1H, dd, J = 15.2, 7.2 Hz) were similar to those of cycloartobiloxanthone.[15] It was apparent that **5** is a dihydrobenzoxanthone derivative having a dihydrofuran ring like that of cycloartobiloxanthone.[15] In addition to the above evidence, the ^1H NMR spectrum of **5** exhibited two aromatic proton signals at δ 6.28 (1H, s) and 6.34 (1H, s), an oxymethine proton signal at δ 5.01 (t, J = 6.4 Hz), two aliphatic proton signals at δ 2.00 (1H, dd, J = 14.4, 6.4 Hz) and 2.31 (1H, dd, J = 14.4, 6.8 Hz), two

Table 2. Cytotoxicity of Compounds **4** and **6** (ED_{50} values in μg/mL)[a]

cell line[b]	A549	Hep 3B	HT-29	MCF-7
4	10.0	3.2	3.9	3.1
6	1.1	21.9	3.1	2.7
5-flurouracil[c]	0.4	0.6	0.2	0.2

[a] For significant activity, an $ED_{50} \leq 4.0$ μg/mL is required. Compounds **1**−**3**, **5**, artonin F, cycloartobiloxanthone, and artonol B were all inactive for all cell lines. [b] Key to all lines: A549 (human lung carcinoma), Hep3B (hepatomacellular carcinoma), HT-29 (human colorectal adenocarcinoma), and MCF-7 (human breast adenocarcinoma). [c] Positive control.

tertiary methyl proton signals at δ 1.36 (s) and 1.48 (s), and a hydroxy-bonded hydroxyl group at δ 13.28. In the ^{13}C NMR spectrum of **5** (Table 1), the chemical shift values were similar to those of the relevant data of cycloartobiloxanthone[15] except for the carbon signals at C-4a, C-5 to C-8, C-8a, and C-14 to C-19. The ^{1}H−^{1}H COSY correlation between H_2-14 and H-15 and the HMBC correlations for H_β-14/C-8 and H-15, H_α-14/C-16, H-15/C-16, and H-16/Me-17 and Me-18 confirmed that a 2,3-dihydroxy-3-methylbutyl group is linked at C-8 in **5**. A NOESY experiment on **5** showed cross-peaks between H_α-9/H-10 and H_α-14/H-15. This suggested that the hydrogen group at C-10 and the hydroxyl group at C-15 are on the α- and β-side of the molecule, respectively. Consequently, the structure of cycloartelastoxanthendiol (**5**) was determined as 5,5a,6-trihydro-1,3,8-trihydroxy-1-methoxy-11-(2′,3′-dihydroxy-3′-methyl-1-butenyl)-5,5,-dimethylbenzofuro[3,3*a*,4:*ab*]xanthen-7-one.

Using a MTT microassay for cytotoxicity, prenylflavonoids **1**−**6**, artonin F, and cycloartobiloxanthone were screened.[16] The results are shown in Table 2. Of these substances, compound **6** exhibited the most potent cytotoxicity against the MCF-7, A549, and HT-29 human cancer cell lines.

Experimental Section

General Experimental Procedures. Optical rotations were obtained on a JASCO model DIP-370 digital polarimeter. UV spectra were obtained on a JASCO model 7800 UV−vis spectrophotometer. IR spectra were recorded on a Perkin-Elmer 2000 FT-IR spectrophotometer. ^{1}H (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Varian Unity-400 NMR spectrophotometer. MS were obtained on a JMS-HX-100 mass spectrometer.

Plant Material. The roots of *Artocarpus elasticus* (4 kg) were collected at Ping-Tung Hsien, Taiwan, in August 2002. A voucher specimen (2006) is deposited in the Laboratory of Medicinal Chemistry, School of Pharmacy, Kaohsiung Medical University.

Extraction and Isolation. The root bark (0.9 kg) of *A. elasticus* was chipped and extracted with CH_2Cl_2 at room temperature. The resultant CH_2Cl_2 extract (230 g) was chromatographed over a silica gel column and eluted with *n*-hexane−EtOAc (5:1) to yield artonin F (16 mg), cycloartobiloxanthone (40 mg), cyclomorusin (130 mg), and **1** (21 mg). Elution with CH_2Cl_2−acetone (50:1) yielded **2** (13 mg), and with $CHCl_3$−acetone (20:1), **4** (17 mg) was obtained, while elution with *n*-hexane−acetone (3:1) yielded **3** (19 mg) and **5** (14 mg). The combined eluates obtained with acetone were further separated with a RP-18 column (30 cm × 10 mm, acetone−H_2O, 3:1) and yielded artonols A (**6**, 9 mg) and B (2 mg). All known compounds were identified by spectroscopic methods and compared with the literature values.[12−15]

Artelastoheterol (1): orange gum; $[\alpha]_D^{28}$ 0° (*c* 0.1, acetone); UV (MeOH) λ_{max} (log ϵ) 210 (4.49), 277 (4.40), 290 (sh) (3.95), 315 (3.61), 437 (4.44) nm; IR (KBr) ν_{max} 3395, 1652, 1620 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.44 (3H, s, Me-18), 1.45 (3H, s, Me-17), 1.66 (3H, s, Me-22), 1.661/1.664 (3H, s, Me-12), 1.81 (3H, s, Me-23), 1.919/1.922 (3H, s, Me-13), 3.45 (2H, m, H-19), 5.22 (1H, t, J = 6.4 Hz, H-20), 5.44 (1H, d, J = 9.2 Hz, H-10), 5.59 (1H, d, J = 10.0 Hz, H-15), 6.18 (1H, d, J = 9.2 Hz, H-9), 6.45 (1H, s, H-3′), 6.69 (1H, d, J = 10.0 Hz, H-14), 7.25 (1H, s, H-6′), 12.80 (1H, s, OH-5); ^{13}C NMR ($CDCl_3$, 100 MHz), see Table 1; EIMS (70 eV) *m/z* 518 ([M − 2]$^+$, 9), 502 ([M − H_2O]$^+$, 48), 447 ([M − H_2O − C_4H_7]$^+$, 100), 391 ([M − H_2O − $(C_4H_7)_2$ − H]$^+$, 18), 261 (21), 216 (7), 205 (29), 153 (17); HREIMS *m/z* [M − H_2O]$^+$ 502.1994 (calcd for $C_{30}H_{30}O_7$, 502.1994).

Artelasticinol (2): orange gum; $[\alpha]_D^{28}$ 0° (*c* 0.1, acetone); UV (MeOH) λ_{max} (log ϵ) 215 (3.90), 273 (3.82), 295 (sh) (3.32), 370 (3.30) nm, (MeOH−$AlCl_3$) 288, 375, 400 nm, (MeOH−NaOAc) 275, 376 nm, (MeOH−NaOMe) unchanged; IR (KBr) ν_{max} 3420, 1651, 1600 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.705/1.709 (3H, s, Me-12), 1.76 (3H, s, Me-17), 1.87 (3H, s, Me-18), 1.982/1.978 (3H, s, Me-13), 3.57 (2H, d, J = 6.4 Hz, H-14), 3.84 (3H, s, OMe-4′), 5.30 (1H, t, J = 6.4 Hz, H-15), 5.45 (2H, d, J = 9.2 Hz, H-10), 6.27 (1H, d, J = 9.2 Hz, H-9), 6.32 (1H, s, H-6), 6.48 (1H, d, J = 2.4 Hz, H-3′), 6.61 (1H, dd, J = 8.8, 2.4 Hz, H-5′), 7.66 (1H, d, J = 8.8, H-6′), 12.78 (1H, brs, OH-5); ^{13}C NMR ($CDCl_3$, 100 MHz), see Table 1; EIMS (70 eV) *m/z* 452 ([M]$^+$, 100), 435 ([M − H_2O]$^+$, 44), 409 ([M − C_3H_6]$^+$, 78), 395 (87), 353 (48), 219 (19), 165 (73), 69 (88), 55 (86); HREIMS *m/z* [M]$^+$ 452.1830 (calcd for $C_{26}H_{28}O_7$, 452.1835).

Cycloartelastoxanthone (3): orange gum; $[\alpha]_D^{28}$ 0° (*c* 0.1, acetone); UV (MeOH) λ_{max} (log ϵ) 210 (4.45), 235 (4.25), 267 (4.10), 285 (sh) (4.08), 420 (4.08) nm; IR (KBr) ν_{max} 3299, 1646, 1600 cm^{-1}; ^{1}H NMR (acetone-d_6, 400 MHz) δ 1.31 (3H, s, Me-12), 1.42 (6H, s, Me-27, 28), 1.44 (3H, s, H-17), 1.63 (1H, s, H-22), 1.64 (3H, s, Me-13), 1.73 (2H, m, H-18), 1.79 (1H, s, H-23), 2.13 (2H, m, H-19), 2.34 (1H, t, J = 15.2 Hz, H-9α), 3.20 (1H, dd, J = 15.2, 7.2 Hz, H-9β), 3.31 (2H, d, J = 7.2 Hz, H-14), 3.39 (1H, dd, J = 15.2, 7.2 Hz, H-10), 5.12 (1H, m, H-20), 5.23 (1H, t, J = 7.2 Hz, H-15), 5.63 (1H, d, J = 10.0 Hz, H-25), 6.39 (1H, s, H-3′), 6.99 (1H, d, J = 10.0 Hz, H-24), 13.70 (1H, s, OH-5); ^{13}C NMR (acetone-d_6, 100 MHz), see Table 1; EIMS (70 eV) *m/z* 570 ([M]$^+$, 10), 555 ([M − Me]$^+$, 3), 515 ([M − a]$^+$, 11), 487 ([M − b]$^+$, 64), 431 (6), 215 (13), 69 (100); HREIMS *m/z* [M]$^+$ 570.2623 (calcd for $C_{35}H_{38}O_7$, 570.2618).

Artelastoxanthone (4): orange gum; $[\alpha]_D^{28}$ −67° (*c* 0.2, acetone); UV (MeOH) λ_{max} (log ϵ) 210 (4.54), 265 (sh) (4.45), 275 (4.50), 390 (4.08) nm; IR (KBr) ν_{max} 3174, 1652, 1613 cm^{-1}; ^{1}H NMR (acetone-d_6, 400 MHz) δ 1.45 (3H, s, Me-18), 1.47 (3H, s, Me-17), 1.77 (3H, s, H-13), 2.45 (1H, dd, J = 16.0, 6.4 Hz H-9α), 3.38 (1H, dd, J = 16.0, 2.0 Hz, H-9β), 3.98 (1H, d, J = 6.4 Hz, H-10), 4.31 (1H, s, H-12α), 4.64 (1H, s, H-12β), 5.75 (1H, d, J = 10.0 Hz, H-15), 6.28 (1H, d, J = 2.4 Hz, H-6), 6.58 (1H, d, J = 2.4 Hz, H-8), 6.76 (1H, d, J = 10.0 Hz, H-14), 7.58 (1H, s, OH-5′), 8.02 (1H, s, OH-2′), 9.63 (1H, s, OH-7), 13.17 (1H, s, OH-5); ^{13}C NMR (acetone-d_6, 100 MHz), see Table 1; FABMS *m/z* 435 ([M + 1]$^+$); HRESIMS *m/z* [M + 1]$^+$ 435.1441 (calcd for $C_{35}H_{39}O_7$, 435.1444).

Cycloartelastoxanthendiol (5): yellowish powder; $[\alpha]_D^{28}$ −49° (*c* 0.5, MeOH); UV (MeOH) λ_{max} (log ϵ) 210 (4.57), 265 (3.34), 312 (sh) (2.78), 380 (4.08) nm; IR (KBr) ν_{max} 3394, 1651, cm^{-1}; ^{1}H NMR (pyridine-d_5, 400 MHz) δ 1.35 (3H, s, Me-12), 1.36 (3H, s, Me-17), 1.48 (3H, s, H-18), 1.68 (3H, s, H-13), 2.00 (1H, dd, J = 14.4, 6.4 Hz H-14α), 2.31 (1H, dd, J = 14.4, 6.4 Hz, H-14β), 2.44 (1H, t, J = 15.2 Hz, H-10), 3.23 (1H, dd, J = 15.2, 7.2 Hz, H-9β), 3.38 (3H, s, MeO-19), 3.43 (1H, dd, J = 15.2, 7.2 Hz, H-9α), 5.01 (1H, t, J = 6.4 Hz, H-15), 6.28 (1H, s, H-6), 6.34 (1H, s, H-3′), 13.28 (1H, s, OH-5); ^{13}C NMR (pyridine-d_5, 100 MHz), see Table 1; FABMS *m/z* 467 ([M − H_2O + 1]$^+$); HRESIMS *m/z* [M − H_2O + 1]$^+$ 467.1708 (calcd for $C_{26}H_{27}O_8$, 467.1706).

Cytotoxicity Bioassays. Assays for cytotoxicity against A549 (human lung carcinoma), MCF-7 (human breast adenocarcinoma), Hep 3B (hepatomacellular carcinoma), and HT-29 (human colorectal adenocarcinoma) were performed by the method described previously.[16]

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Supporting Information Available: A figure showing the MS fragmentation of **3** is available free of charge via the Internet at http://pubs.acs.org.

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