# Cytotoxic Prenylflavonoids from *Artocarpus elasticus*

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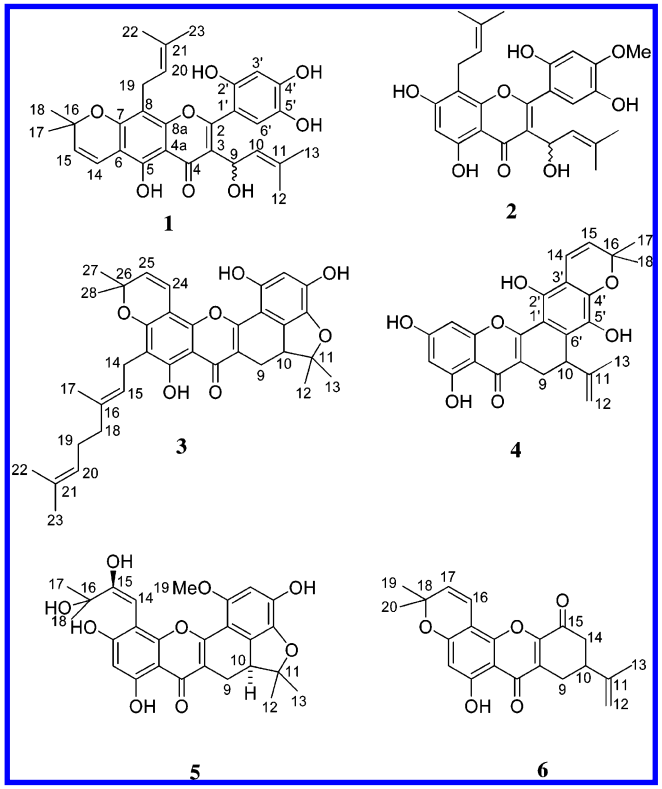
Five new prenylated flavonoids, artelastoheterol (**1**), artelasticinol (**2**), cycloartelastoxanthone (**3**), artelastoxanthone (**4**), and cycloartelastoxanthendiol (**5**), along with five known compounds, were isolated from the root bark of *Artocarpus elasticus*. The structures of **1**−**5** 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 $\mu$g/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 ($\delta$ 178.8), a quaternary carbon ($\delta$ 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 [$\delta$ 12.80 (1H, s)], a 2,2-dimethylpyran ring [$\delta$ 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 [$\delta$ 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 [$\delta$ 1.922 and 1.919, 1.664 and 1.661], an oxymethine proton [$\delta$ 6.18 (1H, bd, $J$ = 9.2 Hz)], an olefinic proton [$\delta$ 5.44 (1H, m)] on a 1-hydroxy-3,3-dimethylallyl group,[5] and two aromatic protons [$\delta$ 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, $\delta$ 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 [$\delta$ 12.78 (1H, brs)], a 1-hydroxy-3,3-dimethylallyl group[5] [$\delta$ 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 ($\delta$ 1.982, 1.978, 1.709, and 1.705)], a 3,3-dimethylallyl group [$\delta$ 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 [$\delta$ 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 $\delta$ 3.84 and a singlet aromatic proton at $\delta$ 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 [$\lambda_{max}$ 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 [$\delta$ 13.70 (1H, s), 9.17 (1H, brs), and 8.94 (1H, brs)], a 2,2-dimethylpyran ring [$\delta$ 6.99 (1H, d, $J$ = 10.0 Hz), 5.63 (1H, d, $J$ = 10.0 Hz), and 1.42 (6H, s)], a geranyl group [$\delta$ 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 [$\delta$ 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 [$\delta$ 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 $\delta$ 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 [$\delta$ 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 $\delta$ 1.35 and 1.68 (3H, s, each) and an ABX system of proton signals at $\delta$ 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 $\delta$ 6.28 (1H, s) and 6.34 (1H, s), an oxymethine proton signal at $\delta$ 5.01 (t, $J$ = 6.4 Hz), two aliphatic proton signals at $\delta$ 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 $\mu$g/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 $ED_{50} \leq 4.0$ $\mu$g/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 $\delta$ 1.36 (s) and 1.48 (s), and a hydroxy-bonded hydroxyl group at $\delta$ 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 $H_\beta$-14/C-8 and H-15, $H_\alpha$-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 $H_\alpha$-9/H-10 and $H_\alpha$-14/H-15. This suggested that the hydrogen group at C-10 and the hydroxyl group at C-15 are on the α- and $\beta$-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) $\lambda_{max}$ (log $\epsilon$) 210 (4.49), 277 (4.40), 290 (sh) (3.95), 315 (3.61), 437 (4.44) nm; IR (KBr) $\nu_{max}$ 3395, 1652, 1620 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 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) $\lambda_{max}$ (log $\epsilon$) 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) $\nu_{max}$ 3420, 1651, 1600 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 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) $\lambda_{max}$ (log $\epsilon$) 210 (4.45), 235 (4.25), 267 (4.10), 285 (sh) (4.08), 420 (4.08) nm; IR (KBr) $\nu_{max}$ 3299, 1646, 1600 cm$^{-1}$; $^1$H NMR (acetone-$d_6$, 400 MHz) $\delta$ 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-9$\beta$), 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) $\lambda_{max}$ (log $\epsilon$) 210 (4.54), 265 (sh) (4.45), 275 (4.50), 390 (4.08) nm; IR (KBr) $\nu_{max}$ 3174, 1652, 1613 cm$^{-1}$; $^1$H NMR (acetone-$d_6$, 400 MHz) $\delta$ 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-9$\beta$), 3.98 (1H, d, $J$ = 6.4 Hz, H-10), 4.31 (1H, s, H-12α), 4.64 (1H, s, H-12$\beta$), 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) $\lambda_{max}$ (log $\epsilon$) 210 (4.57), 265 (3.34), 312 (sh) (2.78), 380 (4.08) nm; IR (KBr) $\nu_{max}$ 3394, 1651, cm$^{-1}$; $^1$H NMR (pyridine-$d_5$, 400 MHz) $\delta$ 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-14$\beta$), 2.44 (1H, t, $J$ = 15.2 Hz, H-10), 3.23 (1H, dd, $J$ = 15.2, 7.2 Hz, H-9$\beta$), 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.

## References and Notes

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