Tirucallane Triterpenoids from *Cornus walteri*

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Twelve new tirucallane triterpenoids, named cornusalterins A−L (**1**−**12**), and two known tirucallane triterpenoids, deoxyflindissone (**13**) and (−)-leucophyllone (**14**), were isolated from a MeOH extract of stems and stem bark of *Cornus walteri*. The structures of the new compounds were determined by spectroscopic methods, including 1D and 2D NMR analyses. Compounds **12** and **13**, possessing a tetrahydrofuran ring in the side chain, exhibited significant cytotoxic activity against the A549, SK-OV-3, SK-MEL-2, and XF498 cell lines.

The genus *Cornus* comprises a group of 30−50 species of mostly deciduous trees and shrubs that contain a variety of cytotoxic constituents such as iridoid glycosides, polyphenols, triterpenoids, and lignans from the fruits of *Cornus kousa*[1−4] and the benzofuranone derivative halleridone from *Cornus controversa*.[5] *Cornus walteri* Wanger (Cornaceae) is a deciduous shrub that grows in valley areas of Asia, particularly China and Korea.[6] The fruits and leaves are used to treat inflammation of the skin or boils caused by lacquer poison in Chinese folk medicine.[7] In Korean folk medicine, the leaves have been used as an antidiarrheal.[8] Previous phytochemical investigations on *C. walteri* led to the isolation of gallic acid and flavonoids.[7,8] Extracts of *C. walteri* inhibited NO production in lipopolysaccharide (LPS)-activated macrophages[9] and were reported to have elastase and tyrosinase inhibitory activity[10] and antihyperglycemic and antiobesity effects.[11]

In our search for bioactive constituents from Korean medicinal plants, we investigated a methanol extract of stems and stem bark of *C. walteri* as the extract showed considerable cytotoxicity against A549, SK-OV-3, and SK-MEL-2 cells. Bioassay-guided fractionation of the MeOH extract resulted in the isolation of 12 new tirucallane triterpenoids named cornusalterins A−L (**1**−**12**) and the known tirucallane triterpenoids (**13** and **14**). Their structures were determined using spectroscopic data, including 1D and 2D NMR. Compounds **1**−**14** were evaluated for cytotoxic activity against four human cancer cell lines. We report herein the isolation, structural elucidation (**1**−**12**), and cytotoxicity of all of the isolated compounds.

Results and Discussion

Cornusalterin A (**1**), a white, amorphous powder, had the molecular formula $C_{31}H_{52}O_2$, as obtained from positive-ion HR-FABMS. The IR spectrum of **1** indicated the presence of OH (3404 cm^{-1}) and C=C double-bond groups (1658 cm^{-1}). The ^1H NMR data (Table 1) showed the presence of seven tertiary methyl [δ_H 0.76, 0.85, 0.87, 0.98, 0.99, 1.26, and 1.26 (each 3H, s)], a secondary methyl [δ_H 0.84 (3H, d, J = 6.0 Hz)], an *O*-methyl [δ_H 3.16 (3H, s)], an oxygenated methine [δ_H 3.25 (1H, dd, J = 11.5, 4.0 Hz)], and three olefinic [δ_H 5.27 (1H, d, J = 2.0 Hz), 5.40 (1H, d, J = 16.0 Hz), and 5.53 (1H, ddd, J = 16.0, 8.0, 5.5 Hz)] proton signals. The ^{13}C NMR spectrum indicated 31 carbon resonances, which were classified by DEPT and HMQC experiments as one trisubstituted double bond (δ_C 118.1 and 145.9), one disubstituted double bond (δ_C 129.4 and 136.5), nine methyls, including an *O*-methyl at δ_C 50.4, eight methylenes, five methines, including an oxygenated methine at δ_C 79.4, and five quaternary carbons, including an oxygenated quaternary carbon at δ_C 75.0. Comparison of its NMR data with those of (−)-leucophyllone (**14**),[12] and the fact that tirucallane triterpenoids were previously isolated from this plant genus,[13] indicated that compound **1** was an analogue of **14**. The CD spectrum of **1** showed a negative (λ_{max} 294 nm) Cotton effect identical to that of **14**, which was identical to the negative Cotton effect of piscidinol A, a tirucallane triterpenoid.[14] The NMR data of **1** and **14** revealed that they possessed the same tetracyclic A−D rings, and the only difference was the signal at C-3 in the NMR data [δ_H 3.25 (1H, dd, J = 11.5, 4.0 Hz); δ_C 79.4 in **1**; δ_C 216.9 in **14**]. This was confirmed by the HMBC experiment showing correlations from the oxymethine proton (δ_H 3.25) to C-1, C-5, C-28, and C-29. The HMBC spectrum indicated the presence of an OCH_3 group at C-25. The β-orientation of OH-3 was deduced from correlations of H-3/H-28 and H-3/H-5 in the NOSEY spectrum.

Cornusalterin B (**2**) had the molecular formula $C_{31}H_{52}O_2$ by HRFABMS. Inspection of the ^1H and ^{13}C NMR data of **2** revealed that these data were again very similar to those of **14**,[12] except for the chemical shifts of a methylene [δ_H 1.29 and 1.52 (each 1H, m); δ_C 35.8] in **2** taking the place of C-7 in **14**. This indicated that the typical $\Delta^{7,8}$ double bond in **14** was saturated in **2**. The structure was supported by HMBC correlations from H-5 to C-7 and from H-30 to C-8, and the configuration of **2** was determined by analysis of the NOESY spectrum and CD data to be the same as **14**.

Analysis of the ^1H and ^{13}C NMR data of **3** ($C_{31}H_{54}O_2$, cornusalterin C) revealed that **3** possessed a tirucallane-type triterpenoid skeleton similar to that of **2**. The difference was that one oxygenated methine [δ_H 3.22 (1H, dd, J = 11.5, 4.0 Hz); δ_C 79.1] in **3** replaced a ketone at C-3 in **2**. The HMBC spectrum showed correlations from H-3 to C-1, C-5, C-28, and C-29, supporting the presence of an OH at C-3 in the structure.

Cornusalterin D (**4**) had the molecular formula $C_{30}H_{46}O_1$. Inspection of the ^1H and ^{13}C NMR data revealed that the tetracyclic part of the molecule was nearly identical to that of **14**,[12] and the side chain was similar to that of (23*E*)-cucurbita-5,23,25-triene-3β,7β-diol.[15] The (23*E*)-$\Delta^{23,25}$-conjugated diene C-8 side chain of **4** was determined by the NMR data [δ_H 1.83 (3H, s, H-26), 4.84 (2H, br s, H-27), 5.61 (1H, ddd, J = 15.5, 7.5, 7.5 Hz, H-23), and 6.09 (1H, d, J = 15.5 Hz, H-24); δ_C 114.2 (C-27), 130.0 (C-23), 134.1 (C-24), and 142.4 (C-25)] and was confirmed by the HMBC experiment showing correlations between H-23 and C-20, C-22, and C-25 and between H-27 and C-24, C-25, and C-26.

The molecular formula of cornusalterin E (**5**) was $C_{30}H_{48}O_1$. The ^1H and ^{13}C NMR data of **5** (Tables 1 and 2) were similar to those of **4**, except that the proton and carbon resonances of two double bonds in the side chain were absent, and resonances of the $\Delta^{1,2}$-

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Chart 1

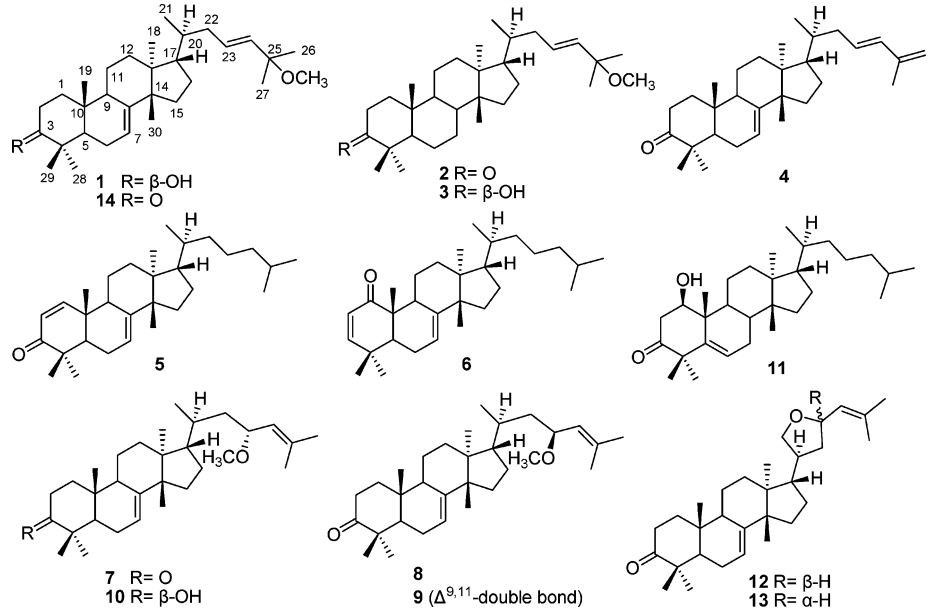

Table 1. ^{1}H NMR Data of Compounds **1**, **5**−**7**, and **12** ($CDCl_3$, 500 MHz, δ in ppm, J in Hz)[a]

H	1	5	6	7	12
1α	1.15, m	6.93, d (10.0)		1.43, m	1.44, m
1β	1.65, m			1.97, m	1.97, m
2α	1.65, m	5.92, d (10.0)	5.80, d (10.0)	2.24, ddd (14.5, 5.0, 5.0)	2.23, ddd (14.5, 5.0, 5.0)
2β	1.74, m			2.76, ddd (14.5, 14.5, 5.0)	2.75, ddd (14.5, 14.5, 5.0)
3α	3.25, dd (11.5, 4.0)		6.50, d (10.0)		
5α	1.32, dd (11.5, 6.0)	2.06, m	2.12, m	1.74, m	1.72, m
6	2.20, m, 2.14, m	2.19, m, 2.08, m	2.22, m, 2.06, m	2.11, m, 2.09, m	2.11, m, 2.09, m
7	5.27, d (2.0)	5.58, m	5.56, m	5.31, m	5.31, m
9α	2.23, m	2.55, m	2.82, m	2.28, m	2.31, m
11α	1.53, m	1.57, m	1.60, m	1.68, m	1.61, m
11β	1.17, m	1.09, m	1.26, m	1.26, m	1.25, m
12α	1.44, m	1.53, m	1.58, m	1.52, m	1.52, m
12β	1.51, m	1.62, m	1.64, m	1.58, m	1.58, m
15α	1.53, m	1.54, m	1.59, m	1.50., m	1.50, m
15β	1.79, m	1.70, m	1.67, m	1.78, m	1.79, m
16α	1.32, m	1.56, m	1.56, m	1.48, m	1.46, m
16β	1.96, m	1.81, m	1.70, m	1.97, m	1.87, m
17	1.49, m	1.32, m	1.37, m	1.46, m	1.46, m
18	0.85, s	0.98, s	1.06, s	0.85, s	0.84, s
19	0.76, s	1.04, s	1.02, s	1.01, s	1.01, s
20	1.55, m	1.53, m	1.61, m	1.70, m	1.85, m
21	0.84, d (6.0)	1.06, d (6.5)	1.07, d (6.5)	0.90, d (6.5)	3.44, dd (9.0, 8.0) 3.91, dd (8.0, 7.5)
22	2.39, m, 1.74, m	1.24, m, 1.09, m	1.25, m, 1.09, m	1.85, m, 0.89, m	1.79, m, 1.65, m
23	5.53, ddd (16.0, 8.0, 5.5)	1.22, m, 1.25, m	1.21, m, 1.24, m	3.94, ddd (9.0, 9.0, 2.0)	4.56, m
24	5.40, d (16.0)	1.06, m, 1.10, m	1.08, m, 1.11, m	5.04, br d (9.0)	5.19, br d (8.5)
26	1.26, s	0.87, d (6.5)	0.91, d (6.0)	1.69, s	1.68, s
27	1.26, s	0.87, d (6.5)	0.91, d (6.0)	1.75, s	1.72, s
28	0.99, s	1.14, s	1.08, s	1.06, s	1.05, s
29	0.87, s	1.11, s	1.09, s	1.12, s	1.11, s
30	0.98, s	1.06, s	1.07, s	1.02, s	1.01, s
OMe	3.16, s			3.21, s	

[a] The assignments were based on DEPT, HMQC, and HMBC experiments.

double bond [δ_H 6.93 (1H, d, J = 10.0 Hz); δ_C 155.4 and δ_H 5.92 (1H, d, J = 10.0 Hz); δ_C 126.0] were present in **5**. In the HMBC spectrum, correlations of H-1/C-3, C-5, C-19, H-2/C-4, C-10, H-28/C-3, C-5, H-29/C-3, C-5, and H-19/C-1, C-5, C-9, C-10 revealed the presence of a double bond at C-1/C-2 and a ketone at C-3. HMBC correlations of H-21/C-17, C-22, H-26/C-24, C-25, H-27/C-24, C-25, and H-30/C-8, C-13, C-15 were also observed. This evidence confirmed that **5** and lanosta-1,7-dien-3-one shared the same planar structure.[16] However, the strongly negative optical rotation of **5** suggested that it was a tirucallane-type triterpenoid,[12,13] since lanosta-1,7-dien-3-one had a positive optical rotation value.[16] This conclusion was supported by analysis of the NOESY spectrum (correlations of H-19/H-30, H-30/H-17, H-5/H-9, H-9/H-18, and H-17/H-21) and CD data.

Cornusalterin F (**6**) exhibited a molecular formula of $C_{30}H_{48}O_1$. Analysis of the ^{1}H and ^{13}C NMR data of **6** (Tables 1 and 2) revealed that **6** possessed a tirucallane-type triterpenoid skeleton similar to that of **5**. The major differences were the chemical shifts of a double bond [δ_H 5.80 and 6.50 (each 1H, d, J = 10.0 Hz); δ_C 126.0 and 157.2] in **6** instead of those of the double bond [δ_H 5.92 and 6.93 (each 1H, d, J = 10.0 Hz); δ_C 126.0 and 155.4] in **5**. HMBC correlations from H-19 (δ_H 1.02) to C-1 (δ_C 206.0), C-9 (δ_C 41.8), and C-10 (δ_C 38.1), from H-28 (δ_H 1.08) to C-3 (δ_C 157.2), and

Table 2. ^{13}C NMR Data of Compounds **1**, **5**−**7**, and **12** ($CDCl_3$, 125 MHz, δ in ppm)

carbon	1	5	6	7	12
1	37.4 t	155.4 d	206.0 s	38.7 t	38.4 t
2	27.9 t	126.0 d	126.0 d	35.2 t	34.8 t
3	79.4 d	205.1 s	157.2 d	217.0 s	216.7 s
4	39.2 s	45.2 s	35.2 s	48.0 s	47.8 s
5	50.8 d	48.4 d	47.1 d	52.5 d	52.4 d
6	24.1 t	23.9 t	24.5 t	24.6 t	24.3 t
7	118.1 d	117.7 d	116.7 d	117.9 d	118.1 d
8	145.9 s	145.3 s	146.6 s	146.2 s	145.5 s
9	49.1 d	44.4 d	41.8 d	48.6 d	48.4 d
10	35.1 s	38.3 s	38.1 s	35.1 s	35.1 s
11	18.3 t	17.4 t	19.9 t	18.5 t	17.8 t
12	34.0 t	32.6 t	33.1 t	34.2 t	32.2 t
13	43.8 s	42.0 s	42.3 s	43.7 s	43.9 s
14	51.4 s	55.2 s	55.3 s	51.5 s	50.5 s
15	34.1 t	32.3 t	32.3 t	34.1 t	34.3 t
16	28.5 t	29.4 t	29.5 t	28.6 t	27.3 t
17	53.2 d	55.2 d	55.3 d	54.1 d	51.0 d
18	22.4 q	23.1 q	23.5 q	22.3 q	22.5 q
19	13.3 q	13.6 q	23.8 q	13.0 q	12.7 q
20	36.3 d	35.6 d	35.6 d	32.6 d	43.1 d
21	19.1 q	21.5 q	22.9 q	18.9 q	72.9 t
22	38.5 t	37.9 t	37.1 t	41.7 t	38.6 t
23	129.4 d	24.4 t	24.9 t	75.3 d	75.7 d
24	136.5 d	38.2 t	38.3 t	127.4 d	126.1 d
25	75.0 s	29.4 d	29.2 d	134.7 s	135.7 s
26	26.0 q	22.7 q	22.7 q	18.3 q	18.0 q
27	26.3 q	22.7 q	22.7 q	26.0 q	25.8 q
28	27.8 q	24.5 q	25.2 q	24.8 q	24.5 q
29	14.9 q	21.5 q	24.9 q	21.8 q	21.5 q
30	27.5 q	25.9 q	25.9 q	27.6 q	27.2 q
OMe	50.4 q			55.9 q	

from H-29 (δ_H 1.09) to C-3 (δ_C 157.2) revealed the presence of a ketone at C-1 and a double bond at C-2/C-3.

The molecular formula of cornusalterin G (**7**) was established to be $C_{31}H_{50}O_2$. Its NMR data (Tables 1 and 2) resembled those of **14**,[12] except for some differences in the side chain. The chemical shifts from C-20 to C-27 in the side chain were similar to those of 23-hydroxycycloart-24-en-3-one.[17] The chemical shifts of C-23 in **7** [δ_H 3.94 (1H, ddd, J = 9.0, 9.0, 2.0 Hz); δ_C 75.3] were shifted as compared with those of C-23 in 23-hydroxycycloart-24-en-3-one [δ_H 4.30−4.70 (1H, m); δ_C 65.8],[17] indicating that an OCH_3 group [δ_H 3.21 (3H, s); δ_C 55.9] instead of an OH group at C-23 in **7** was present. The side chain was confirmed by the HMBC experiment (correlations of H-21/C-17, C-22, H-23/C-20, C-24, C-25, and H-24/C-22, C-23, C-26, C-27). In addition, the HMBC correlation between *O*-methyl (δ_H 3.21) and C-23 (δ_C 75.3) indicated that the OCH_3 group was located at C-23. Finally, the absolute configuration of C-23 was determined using demethylation[18] and modified Mosher's method.[19] Compound **7** was reacted with trimethylsilyl iodide to give 3-oxotirucalla-7,24-dien-23-ol (**7a**), and then treatment of **7a** with (*R*)- and (*S*)-MTPA-Cl gave the (*S*)- and (*R*)-MTPA esters **7s** and **7r**, respectively. The ^1H NMR signals of the two MTPA esters were assigned on the basis of their $^1H-^1H$ COSY spectra, and the $\Delta\delta_{H(S-R)}$ values were then calculated (see Supporting Information). The results indicated that the absolute configuration of C-23 was *R*, which was also supported by NOSEY correlations of H-23/H-17, H-21 and *O*-methyl/H-18.

Inspection of the ^1H and ^{13}C NMR data of **8** ($C_{31}H_{50}O_2$, cornusalterin H) revealed that these data were very similar to those of **7**, except for the chemical shifts from C-23 to C-25 [δ_H 3.93 (1H, ddd, J = 9.5, 9.5, 4.0 Hz) and 4.93 (1H, br d, J = 9.5 Hz); δ_C 76.3 (C-23), 126.0 (C-24), and 136.9 (C-25) in **8**; δ_H 3.94 (1H, ddd, J = 9.0, 9.0, 2.0 Hz) and 5.04 (1H, br d, J = 9.0 Hz); δ_C 75.3 (C-23), 127.4 (C-24), and 134.7 (C-25) in **7**]. Analysis of the 2D NMR data of **8** (HMQC, HMBC, and NOESY) led to unambiguous ^1H and ^{13}C NMR assignments and confirmed **8** to be the 23-epimer of **7**.

Cornusalterin I (**9**) had the molecular formula $C_{31}H_{48}O_2$. The ^1H and ^{13}C NMR data of **9** were very similar to those of **8**, except for the presence of the additional signals assignable to a double bond [δ_H 5.42 (1H, m, H-11); δ_C 114.0 (C-11) and 145.8 (C-9)] in **9**. This $\Delta^{9,11}$ double bond in **9** was confirmed by HMBC correlations from H-7 to C-9 (δ_C 145.8), from H-11 to C-8 (δ_C 142.2), C-10 (δ_C 35.0), and C-13 (δ_C 43.5), and from H-19 to C-9 (δ_C 145.8). Similarly, as described for **7**, the absolute configuration of C-23 in **9** was determined using demethylation[18] and modified Mosher's method,[19] which proved the *S*-configuration for C-23 (see details in the Supporting Information). In addition, the absolute configuration of C-23 in **8** was also determined to be *S* because the chemical shifts and coupling constants of H-23 and H-24 of **8** were very similar to those of **9**. This configuration of **8** was also supported by NOESY correlations of *O*-methyl/H-17 and *O*-methyl/H-21.

The NMR data of **10** ($C_{31}H_{52}O_2$, cornusalterin J) resembled those of **7**, except for signals of an oxygenated methine [δ_H 3.23 (1H, dd, J = 11.5, 4.0 Hz); δ_C 79.2] in **10**. The HMBC spectrum showed correlations from H-3 to C-1, C-5, C-28, and C-29, suggesting the presence of an OH at C-3 in the structure. A β-orientation of OH-3 was determined by NOSEY correlations of H-3/H-28 and H-3/H-5. The absolute configuration of C-23 was determined to be *R* on the basis of the fact that the chemical shifts and splitting patterns of H-23 and H-24 of **10** were very similar to those of **7**.

Cornusalterin K (**11**) gave a molecular formula of $C_{30}H_{50}O_2$. The ^1H and ^{13}C NMR data of **11** were compatible with **5**, except that the proton and carbon resonances of the $\Delta^{1,2}$ double bond were absent, and resonances of one oxygenated methine [δ_H 3.52 (1H, dd, J = 12.0, 4.5 Hz); δ_C 78.9] and one methylene [δ_H 2.46 (1H, dd, J = 12.0, 4.5 Hz), 2.97 (1H, dd, J = 12.0, 12.0 Hz); δ_C 45.6] were present in **11**. The structure of the tetracyclic A and B rings was verified by HMBC correlations from H-1 to C-19, from H-2 to C-1, C-3, C-4, and C-10, from H-19 to C-1, C-5, and C-9, from H-28 to C-3 and C-5, and from H-29 to C-3 and C-5, confirming the presence of an OH at C-1, a ketone at C-3, and a $\Delta^{5,6}$ double bond in the structure. The coupling constants of H-1 (dd, $J_{1,2\alpha}$ =

4.5 Hz and $J_{1,2\beta}$ = 12.0 Hz) observed in the ^{1}H NMR spectrum indicated a β-orientation of OH-1, which was confirmed by NOESY correlations of H-1/H-9 and H-1/H-28.

The molecular formula of cornusalterin L (**12**) was determined to be $C_{30}H_{46}O_2$. The ^{1}H and ^{13}C NMR data of **12** (Tables 1 and 2) suggested that **12** had the same triterpene skeleton as **13**.[13,20] The chemical shifts of H-21 [δ_H 3.44 (1H, dd, J = 9.0, 8.0 Hz) and 3.91 (1H, dd, J = 8.0, 7.5 Hz)] and H-23 [δ_H 4.56 (1H, m)] suggested the presence of an epoxy function at these positions, forming a tetrahydrofuran ring in the side chain.[20] The structure was confirmed by HMBC correlations from H-21 to C-17, C-22, and C-23, from H-23 to C-20, C-21, and C-25, and from H-24 to C-22, C-26, and C-27. The chemical shifts of H-21 and H-23 in the side chain of **12** differed from those of **13**, indicating that **12** is a stereoisomer of **13**. The NOESY spectrum of **13** showed a correlation from H-20 to H-23, but that of **12** did not. Moreover, the CD spectrum of **12** showed a positive (λ_{max} 258 nm) Cotton effect and that of **13** showed a negative (λ_{max} 259 nm) Cotton effect. The remaining configuration of **12** was determined to be the same as **13** by analysis of the NOESY and CD data. In addition, full NMR data of **13** were assigned using 2D NMR data (including HMQC, HMBC, and NOESY) because the published ^{13}C NMR data of 21,23-epoxytirucalla-7,24-diene-3-one were not in good agreement with those of **13**.[13]

The known compound **14** was identified by comparison of spectroscopic data with reported data.[12] Compound **14** showed the strongly negative specific optical rotation value $[\alpha]_D^{25}$ −102.3 (*c* 0.93, $CHCl_3$) and a negative (λ_{max} 295 nm) Cotton effect.

Cytotoxic activities of compounds **1**−**14** against the A549, SK-OV-3, SK-MEL-2, and XF498 human cancer cell lines were evaluated using the SRB assay.[21] Compounds **12** and **13**, possessing a tetrahydrofuran ring in the side chain, exhibited significant cytotoxic activity against the A549, SK-OV-3, SK-MEL-2, and XF498 cell lines (IC_{50}(**12**): 4.29, 3.82, 4.73, and 5.81 μM, and IC_{50}(**13**): 4.02, 3.64, 6.07, and 5.10 μM, respectively). The other compounds were essentially noncytotoxic (see Supporting Information).

Experimental Section

General Experimental Procedures. Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected. Optical rotations were measured on a JASCO P-1020 polarimeter. CD spectra were measured on a JASCO J-715 spectropolarimeter. IR spectra were recorded on a Bruker IFS-66/S FT-IR spectrometer. UV spectra were obtained on a Varian Cary 5000 UV−vis−NIR spectrophotometer. NMR spectra were recorded on a Varian UNITY INOVA 500 NMR spectrometer operating at 500 MHz (^{1}H) or 125 MHz (^{13}C), with chemical shifts given in ppm (δ). FAB and HR-FAB mass spectra were obtained on a JEOL JMS700 mass spectrometer. Preparative HPLC was performed using a Gilson 306 pump with a Shodex refractive index detector. Chromatographic separation was performed on an Apollo Silica 5 μm column (250 × 10 mm i.d.) or Econosil RP-18 10 μm column (250 × 10 mm i.d.). Silica gel 60 and RP-C_{18} silica gel (Merck Co., Germany, 70−230 and 230−400 mesh) were used for column chromatography. TLC was performed using Merck precoated silica gel F_{254} plates and RP-18 F_{254s} plates. Low-pressure liquid chromatography was performed over a LiChroprep Lobar-A Si gel 60 (240 × 10 mm i.d.) column with a FMI QSY-0 pump (ISCO).

Plant Material. Stems and stem bark of *C. walteri* were collected on Jeju Island, Korea, in October 2005, and the plant was identified by one of the authors (K.R.L.). A voucher specimen (SKKU 2005-10a) was deposited in the herbarium of the School of Pharmacy, Sungkyunkwan University, Suwon, Korea.

Extraction and Isolation. Stems and stem bark of *C. walteri* (2.5 kg) were dried, chopped, and extracted with 80% MeOH (2 × 6 h) under reflux and filtered. The filtrate was evaporated under vacuum to obtain a MeOH extract (220 g), which was suspended in distilled H_2O (7.2 L) and then successively partitioned with *n*-hexane, $CHCl_3$, and *n*-BuOH, yielding 9.5, 25.0, and 43.0 g of residue, respectively. The *n*-hexane-soluble fraction showed significant cytotoxic activity against the A549, SK-OV-3, and SK-MEL-2 cell lines using a sulforhodamine B (SRB) assay. The *n*-hexane-soluble fraction was chromatographed on a silica gel (230−400 mesh, 300 g) column eluted with *n*-hexane−EtOAc (3:1 → 1:1, gradient system) to yield fractions H1−H5. Fraction H1 (3.3 g) was chromatographed on an RP-C_{18} silica gel (230−400 mesh, 100 g) column eluted with 100% MeOH to give subfractions H11−H15. Fraction H13 (800 mg) was subjected to silica gel CC (*n*-hexane−EtOAc, 7:1) and preparative RP-HPLC using 100% MeOH to yield compounds **2** (10 mg) and **8** (5 mg). Fraction H14 (300 mg) was subjected to a LiChroprep Lobar-A Si gel 60 column (*n*-hexane−EtOAc, 16:1) and then normal-phase HPLC using *n*-hexane−EtOAc (12:1) to afford compounds **7** (12 mg) and **14** (30 mg). Compounds **5** (15 mg) and **6** (5 mg) were obtained from fraction H15 (100 mg) by HPLC using *n*-hexane−EtOAc (20:1). Fraction H2 (2.5 g) was chromatographed on an RP-C_{18} silica gel (230−400 mesh, 100 g) column eluted with 100% MeOH to give subfractions H21−H28. Fraction H24 (300 mg) was subjected to HPLC using *n*-hexane−EtOAc (8:1) to yield compounds **12** (9 mg) and **13** (15 mg). Fraction H25 (80 mg) was separated by HPLC (*n*-hexane−EtOAc, 8:1) to give compounds **9** (13 mg) and **10** (5 mg). Fraction H3 (1.7 g) was chromatographed on an RP-C_{18} silica gel (230−400 mesh, 70 g) column eluted with 100% MeOH to afford subfractions H31−H36. Fraction H33 (400 mg) was subjected to a LiChroprep Lobar-A Si gel 60 column (*n*-hexane−EtOAc, 4:1) to give five subfractions, H331−H335. Fraction H332 (100 mg) was purified by RP-HPLC using 100% MeOH to yield **4** (7 mg). Fraction H34 (120 mg) was fractionated by HPLC (*n*-hexane−EtOAc, 3:1) to give **1** (30 mg), and fraction H35 (100 mg) was separated by HPLC (*n*-hexane−EtOAc, 4:1) to obtain **11** (42 mg). Fraction H4 (1.3 g) was chromatographed on an RP-C_{18} silica gel (230−400 mesh, 50 g) column eluted with 100% MeOH to afford subfractions H41−H45. Fraction H42 (200 mg) was subjected to a silica gel CC (*n*-hexane−EtOAc, 3:1) and purified by preparative HPLC (*n*-hexane−EtOAc, 2:1) to yield **3** (10 mg).

Cornusalterin A (1): white, amorphous powder; mp 115.0−116.0 °C; $[\alpha]_D^{25}$ −98.6 (*c* 0.85, $CHCl_3$); CD (MeOH) λ_{max} ($\Delta\varepsilon$) 294 (−18.0), 279 (+5.3) nm; IR (KBr) ν_{max} 3404, 2949, 1738, 1658, 1461, 1374, 1216, 1032, 696 cm^{-1}; ^{1}H NMR data, see Table 1; ^{13}C NMR data, see Table 2; FABMS *m/z* 456 $[M]^+$; HRFABMS *m/z* 456.3966 $[M]^+$ (calcd for $C_{31}H_{52}O_2$, 456.3967).

Cornusalterin B (2): white, amorphous powder; mp 131.5−132.5 °C; $[\alpha]_D^{25}$ −31.8 (*c* 0.40, $CHCl_3$); CD (MeOH) λ_{max} ($\Delta\varepsilon$) 292 (−16.4), 272 (+2.5) nm; IR (KBr) ν_{max} 2948, 1705, 1657, 1374, 1031, 731 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.51 (1H, ddd, J = 16.0, 8.0, 5.5 Hz, H-23), 5.41 (1H, d, J = 16.0 Hz, H-24), 3.16 (3H, s, OCH_3-25), 2.65 (1H, ddd, J = 14.5, 14.5, 5.0 Hz, H-2β), 2.23 (1H, m, H-22a), 2.06 (1H, ddd, J = 14.5, 5.0, 5.0 Hz, H-2α), 1.84 (1H, m, H-1β), 1.75 (1H, m, H-6a), 1.72 (1H, m, H-22b), 1.71 (2H, m, H-12β, H-16β), 1.59 (1H, m, H-20), 1.57 (1H, m, H-15β), 1.55 (1H, m, H-16α), 1.53 (1H, m, H-6b), 1.52 (2H, m, H-7a, H-11α), 1.50 (1H, m, H-17), 1.42 (1H, m, H-8), 1.35 (1H, m, H-9α), 1.34 (1H, m, H-1α), 1.29 (2H, m, H-7b, H-15α), 1.27 (6H, s, H-26, H-27), 1.22 (1H, m, H-12α), 1.12 (3H, s, H-28), 1.08 (2H, m, H-5α, H-11β), 1.08 (3H, s, H-29), 0.97 (3H, s, H-19), 0.94 (3H, s, H-30), 0.87 (3H, d, J = 6.0 Hz, H-21), 0.85 (3H, s, H-18); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 216.2 (C-3), 136.7 (C-24), 129.2 (C-23), 75.0 (C-25), 55.2 (C-17), 53.2 (C-5), 50.4 (OCH_3-25), 49.5 (C-9), 48.7 (C-14), 47.2 (C-4), 46.7 (C-13), 42.6 (C-8), 38.4 (C-22), 38.3 (C-1), 37.7 (C-20), 35.8 (C-7), 34.8 (C-2), 33.1 (C-15), 32.3 (C-10), 29.6 (C-16), 26.3 (C-27), 26.0 (C-26), 25.1 (C-12), 23.8 (C-28), 21.5 (C-11), 21.0 (C-29), 18.5 (C-6), 18.3 (C-21), 16.1 (C-30), 14.8 (C-18), 14.7 (C-19); FABMS *m/z* 457 $[M + H]^+$; HRFABMS *m/z* 457.4048 $[M + H]^+$ (calcd for $C_{31}H_{53}O_2$, 457.4046).

Cornusalterin C (3): white, amorphous powder; mp 151.0−152.0 °C; $[\alpha]_D^{25}$ −20.5 (*c* 0.45, $CHCl_3$); CD (MeOH) λ_{max} ($\Delta\varepsilon$) 295 (−18.2) nm; IR (KBr) ν_{max} 3390, 2948, 2838, 1657, 1373, 1031, 722 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.65 (1H, ddd, J = 16.0, 8.0, 5.5 Hz, H-23), 5.51 (1H, d, J = 16.0 Hz, H-24), 3.22 (1H, dd, J = 11.5, 4.0 Hz, H-3α), 3.17 (3H, s, OCH_3-25), 2.23 (1H, m, H-22a), 1.72 (3H, m, H-6a, H-12β, H-22b), 1.69 (1H, m, H-2β), 1.67 (1H, m, H-16β), 1.60 (1H, m, H-2α), 1.57 (2H, m, H-16α, H-20), 1.56 (1H, m, H-1β), 1.53 (2H, m, H-7a, H-15β), 1.51 (2H, m, H-6b, H-11α), 1.48 (1H, m, H-17), 1.44 (1H, m, H-8), 1.34 (1H, m, H-9α), 1.28 (2H, m, H-7b, H-15α), 1.28 (6H, s, H-26, H-27), 1.27 (1H, m, H-1α), 1.22 (1H, m, H-12α), 1.15 (3H, s, H-28), 1.06 (1H, m, H-11β), 0.99 (6H, s, H-18, H-30), 0.87 (3H, s, H-29), 0.86 (3H, d, J = 6.0 Hz, H-21), 0.79 (3H, s, H-19), 0.77 (1H, m, H-5α); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 136.4 (C-24),

128.1 (C-23), 79.1 (C-3), 75.6 (C-25), 56.1 (C-5), 54.5 (C-17), 50.9 (C-9), 50.7 (C-14), 50.2 (OCH_3-25), 45.3 (C-13), 40.6 (C-8), 39.2 (C-22), 39.2 (C-4), 37.1 (C-1), 35.7 (C-20), 35.4 (C-7), 33.0 (C-15), 31.7 (C-10), 28.2 (C-16), 27.6 (C-2), 27.6 (C-28), 26.4 (C-29), 26.1 (C-27), 25.8 (C-26), 25.1 (C-12), 21.4 (C-11), 18.4 (C-6), 18.4 (C-21), 15.7 (C-30), 15.7 (C-19), 15.5 (C-18); FABMS *m/z* 459 $[M + H]^+$; HRFABMS *m/z* 459.4209 $[M + H]^+$ (calcd for $C_{31}H_{55}O_2$, 459.4202).

Cornusalterin D (4): white, amorphous powder; mp 105.0−106.0 °C; $[\alpha]_D^{25}$ −136.0 (*c* 0.32, $CHCl_3$); CD (MeOH) λ_{max} ($\Delta\varepsilon$) 293 (−21.5), 269 (+11.8) nm; IR (KBr) ν_{max} 2949, 2836, 1706, 1657, 1453, 1216, 1030, 726 cm^{-1}; UV (MeOH) λ_{max} (log ε) 227 (3.2) nm; ^1H NMR ($CDCl_3$, 500 MHz) δ 6.09 (1H, d, J = 15.5 Hz, H-24), 5.61 (1H, ddd, J = 15.5, 7.5, 7.5 Hz, H-23), 5.31 (1H, d, J = 2.5 Hz, H-7), 4.84 (2H, br s, H-27), 2.74 (1H, ddd, J = 15.0, 15.0, 5.5 Hz, H-2β), 2.31 (1H, m, H-9α), 2.23 (1H, ddd, J = 15.0, 5.5, 5.5 Hz, H-2α), 2.10 (1H, m, H-6a), 2.08 (1H, m, H-6b), 2.01 (1H, m, H-22a), 1.95 (1H, m, H-16β), 1.92 (1H, m, H-1β), 1.83 (3H, s, H-26), 1.76 (1H, m, H-15β), 1.75 (1H, m, H-22b), 1.74 (1H, m, H-5α), 1.63 (1H, m, H-11α), 1.56 (1H, m, H-12β), 1.54 (1H, m, H-15α), 1.53 (1H, m, H-20), 1.52 (1H, m, H-12α), 1.48 (1H, m, H-17), 1.43 (2H, m, H-1α, H-16α), 1.23 (1H, m, H-11β), 1.11 (3H, s, H-29), 1.04 (3H, s, H-28), 1.01 (3H, s, H-30), 1.00 (3H, s, H-19), 0.84 (3H, s, H-18), 0.83 (3H, d, J = 6.5 Hz, H-21); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 217.0 (C-3), 146.1 (C-8), 142.4 (C-25), 134.1 (C-24), 130.0 (C-23), 118.1 (C-7), 114.2 (C-27), 53.4 (C-17), 52.5 (C-5), 51.5 (C-14), 48.6 (C-9), 48.1 (C-4), 43.8 (C-13), 38.8 (C-22), 38.7 (C-1), 36.6 (C-20), 35.2 (C-2), 35.1 (C-10), 34.2 (C-12), 33.9 (C-15), 28.5 (C-16), 27.7 (C-30), 24.8 (C-28), 24.6 (C-6), 22.5 (C-18), 21.8 (C-29), 19.1 (C-26), 18.9 (C-21), 18.5 (C-11), 13.0 (C-19); FABMS *m/z* 423 $[M + H]^+$; HRFABMS *m/z* 423.3628 $[M + H]^+$ (calcd for $C_{30}H_{47}O_1$, 423.3627).

Cornusalterin E (5): white, amorphous powder; mp 102.5−103.5 °C; $[\alpha]_D^{25}$ −84.1 (*c* 0.63, $CHCl_3$); CD (MeOH) λ_{max} ($\Delta\varepsilon$) 296 (−19.0), 256 (+4.1) nm; IR (KBr) ν_{max} 2949, 1669, 1658, 1454, 1029, 724 cm^{-1}; UV (MeOH) λ_{max} (log ε) 223 (3.9) nm; ^1H NMR data, see Table 1; ^{13}C NMR data, see Table 2; FABMS *m/z* 425 $[M + H]^+$; HRFABMS *m/z* 425.3789 $[M + H]^+$ (calcd for $C_{30}H_{49}O_1$, 425.3783).

Cornusalterin F (6): white, amorphous powder; mp 100.0−101.0 °C; $[\alpha]_D^{25}$ −72.1 (*c* 0.41, $CHCl_3$); CD (MeOH) λ_{max} ($\Delta\varepsilon$) 292 (−12.5), 260 (+8.7) nm; IR (KBr) ν_{max} 2950, 1670, 1656, 1454, 1029, 732 cm^{-1}; UV (MeOH) λ_{max} (log ε) 224 (3.9) nm; ^1H NMR data, see Table 1; ^{13}C NMR data, see Table 2; FABMS *m/z* 425 $[M + H]^+$; HRFABMS *m/z* 425.3780 $[M + H]^+$ (calcd for $C_{30}H_{49}O_1$, 425.3783).

Cornusalterin G (7): white, amorphous powder; mp 127.0−128.0 °C; $[\alpha]_D^{25}$ −14.3 (*c* 0.60, $CHCl_3$); CD (MeOH) λ_{max} ($\Delta\varepsilon$) 294 (−22.3) nm; IR (KBr) ν_{max} 2969, 1708, 1657, 1370, 1216, 1056, 1033 cm^{-1}; ^1H NMR data, see Table 1; ^{13}C NMR data, see Table 2; FABMS *m/z* 455 $[M + H]^+$; HRFABMS *m/z* 455.3884 $[M + H]^+$ (calcd for $C_{31}H_{51}O_2$, 455.3889).

Cornusalterin H (8): white, amorphous powder; mp 127.5−128.5 °C; $[\alpha]_D^{25}$ −5.1 (*c* 0.23, $CHCl_3$); CD (MeOH) λ_{max} ($\Delta\varepsilon$) 296 (−20.1) nm; IR (KBr) ν_{max} 2949, 2836, 1707, 1657, 1452, 1030, 713 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 5.31 (1H, m, H-7), 4.93 (1H, br d, J = 9.5 Hz, H-24), 3.93 (1H, ddd, J = 9.5, 9.5, 4.0 Hz, H-23), 3.23 (3H, s, OCH_3-23), 2.76 (1H, ddd, J = 14.5, 14.5, 5.0 Hz, H-2β), 2.29 (1H, m, H-9α), 2.25 (1H, ddd, J = 14.5, 5.0, 5.0 Hz, H-2α), 2.11 (1H, m, H-6a), 2.09 (1H, m, H-6b), 1.97 (1H, m, H-1β), 1.95 (1H, m, H-16β), 1.84 (1H, m, H-22a), 1.79 (1H, m, H-15β), 1.79 (3H, s, H-27), 1.73 (3H, s, H-26), 1.73 (1H, m, H-5α), 1.70 (1H, m, H-20), 1.68 (1H, m, H-11α), 1.58 (1H, m, H-12β), 1.53 (1H, m, H-12α), 1.50 (1H, m, H-15α), 1.47 (2H, m, H-16α, H-17), 1.44 (1H, m, H-1α), 1.26 (1H, m, H-11β), 1.13 (3H, s, H-29), 1.02 (3H, s, H-28), 1.01 (6H, s, H-19, H-30), 0.91 (1H, m, H-22b), 0.86 (3H, d, J = 6.0 Hz, H-21), 0.79 (3H, s, H-18); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 217.0 (C-3), 146.2 (C-8), 136.9 (C-25), 126.0 (C-24), 118.0 (C-7), 76.3 (C-23), 55.4 (OCH_3-23), 53.9 (C-17), 52.5 (C-5), 51.5 (C-14), 48.7 (C-9), 48.1 (C-4), 43.6 (C-13), 41.2 (C-22), 38.7 (C-1), 35.2 (C-2), 35.1 (C-10), 34.3 (C-12), 34.1 (C-15), 33.0 (C-20), 28.5 (C-16), 27.7 (C-30), 26.1 (C-27), 24.8 (C-28), 24.6 (C-6), 22.2 (C-18), 21.8 (C-29), 19.4 (C-21), 18.7 (C-26), 18.5 (C-11), 13.0 (C-19); FABMS *m/z* 455 $[M + H]^+$; HRFABMS *m/z* 455.3890 $[M + H]^+$ (calcd for $C_{31}H_{51}O_2$, 455.3889).

Cornusalterin I (9): white, amorphous powder; mp 120.0−121.0 °C; $[\alpha]_D^{25}$ −83.5 (*c* 0.65, $CHCl_3$); CD (MeOH) λ_{max} ($\Delta\varepsilon$) 294 (−22.5) nm; IR (KBr) ν_{max} 2948, 2835, 1707, 1658, 1452, 1029, 732 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 5.42 (1H, m, H-11), 5.31 (1H, m, H-7), 4.94 (1H, d, J = 10.0 Hz, H-24), 3.94 (1H, ddd, J = 10.0, 10.0, 4.0 Hz, H-23), 3.23 (3H, s, OCH_3-23), 2.74 (1H, ddd, J = 14.5, 14.5, 5.5 Hz, H-2β), 2.27 (1H, ddd, J = 14.5, 5.5, 5.5 Hz, H-2α), 2.24 (1H, m, H-12β), 2.11 (1H, m, H-6a), 2.10 (1H, m, H-6b), 2.02 (1H, m, H-12α), 2.00 (1H, m, H-5α), 1.95 (1H, m, H-1β), 1.81 (1H, m, H-22a), 1.79 (1H, m, H-16β), 1.78 (3H, s, H-27), 1.73 (3H, s, H-26), 1.69 (1H, m, H-20), 1.66 (1H, m, H-15β), 1.50 (1H, m, H-15α), 1.47 (1H, m, H-16α), 1.46 (2H, m, H-1α, H-17), 1.11 (3H, s, H-29), 1.06 (3H, s, H-28), 1.02 (3H, s, H-30), 1.01 (3H, s, H-19), 0.91 (3H, d, J = 6.5 Hz, H-21), 0.89 (1H, m, H-22b), 0.79 (3H, s, H-18); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 216.9 (C-3), 145.8 (C-9), 142.2 (C-8), 133.8 (C-25), 129.8 (C-24), 117.8 (C-7), 114.0 (C-11), 73.5 (C-23), 54.2 (OCH_3-23), 52.3 (C-17), 51.3 (C-5), 48.4 (C-14), 47.8 (C-4), 43.5 (C-13), 42.2 (C-22), 36.4 (C-1), 35.1 (C-12), 35.0 (C-10), 34.9 (C-2), 33.9 (C-20), 33.6 (C-15), 27.4 (C-16), 27.2 (C-30), 25.7 (C-27), 24.5 (C-6), 24.3 (C-28), 22.2 (C-18), 21.6 (C-29), 18.7 (C-21), 18.3 (C-26), 12.7 (C-19); FABMS *m/z* 453 $[M + H]^+$; HRFABMS *m/z* 453.3734 $[M + H]^+$ (calcd for $C_{31}H_{49}O_2$, 453.3733).

Cornusalterin J (10): white, amorphous powder; mp 125.5−126.5 °C; $[\alpha]_D^{25}$ −16.4 (*c* 0.25, $CHCl_3$); CD (MeOH) λ_{max} ($\Delta\varepsilon$) 294 (−14.3) nm; IR (KBr) ν_{max} 3406, 2970, 1739, 1657, 1368, 1216, 1056, 1033 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 5.25 (1H, d, J = 2.0 Hz, H-7), 5.03 (1H, br d, J = 8.5 Hz, H-24), 3.94 (1H, ddd, J = 8.5, 8.5, 2.0 Hz, H-23), 3.23 (1H, dd, J = 11.5, 4.0 Hz, H-3α), 3.20 (3H, s, OCH_3-23), 2.21 (1H, m, H-9α), 2.19 (1H, m, H-6a), 2.15 (1H, m, H-6b), 1.90 (1H, m, H-16β), 1.84 (1H, m, H-22a), 1.76 (2H, m, H-2β, H-15β), 1.74 (3H, s, H-27), 1.71 (1H, m, H-20), 1.69 (1H, m, H-2α), 1.67 (3H, s, H-26), 1.66 (1H, m, H-1β), 1.55 (1H, m, H-15α), 1.53 (1H, m, H-12β), 1.51 (1H, m, H-11α), 1.49 (1H, m, H-17), 1.44 (1H, m, H-12α), 1.34 (1H, m, H-5α), 1.30 (1H, m, H-16α), 1.17 (2H, m, H-1α, H-11β), 0.97 (6H, s, H-28, H-30), 0.90 (3H, d, J = 6.5 Hz, H-21), 0.90 (1H, m, H-22b), 0.86 (3H, s, H-29), 0.84 (3H, s, H-18), 0.74 (3H, s, H-19); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 145.6 (C-8), 133.7 (C-25), 129.9 (C-24), 117.9 (C-7), 79.2 (C-3), 75.6 (C-23), 55.6 (OCH_3-23), 53.1 (C-17), 51.2 (C-14), 50.6 (C-5), 48.8 (C-9), 43.5 (C-13), 42.0 (C-22), 38.9 (C-4), 37.1 (C-1), 34.9 (C-10), 33.9 (C-15), 33.7 (C-12), 32.7 (C-20), 29.1 (C-16), 27.6 (C-28), 27.5 (C-2), 27.4 (C-30), 26.0 (C-27), 23.9 (C-6), 22.2 (C-18), 18.9 (C-21), 18.7 (C-11), 18.6 (C-26), 14.7 (C-29), 13.1 (C-19); FABMS *m/z* 456 $[M]^+$; HRFABMS *m/z* 456.3967 $[M]^+$ (calcd for $C_{31}H_{52}O_2$, 456.3967).

Cornusalterin K (11): white, amorphous powder; mp 132.5−133.5 °C; $[\alpha]_D^{25}$ −71.7 (*c* 0.98, $CHCl_3$); CD (MeOH) λ_{max} ($\Delta\varepsilon$) 294 (−15.4), 250 (+3.4) nm; IR (KBr) ν_{max} 3398, 2928, 2867, 1703, 1462, 1375, 1251, 1041, 822 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 5.51 (1H, m, H-6), 3.52 (1H, dd, J = 12.0, 4.5 Hz, H-1α), 2.97 (1H, dd, J = 12.0, 12.0 Hz, H-2β), 2.46 (1H, dd, J = 12.0, 4.5 Hz, H-2α), 2.07 (1H, m, H-7a), 1.80 (1H, m, H-16β), 1.67 (1H, m, H-12β), 1.61 (1H, m, H-15β), 1.58 (2H, m, H-7b, H-16α), 1.56 (1H, m, H-15α), 1.55 (1H, m, H-11α), 1.53 (1H, m, H-20), 1.51 (1H, m, H-12α), 1.45 (1H, m, H-8), 1.41 (1H, m, H-9α), 1.30 (1H, m, H-17), 1.28 (1H, m, H-22a), 1.26 (1H, m, H-23a), 1.23 (1H, m, H-23b), 1.22 (1H, m, H-11β), 1.12 (1H, m, H-24a), 1.12 (3H, s, H-30), 1.09 (1H, m, H-22b), 1.09 (3H, s, H-19), 1.06 (1H, m, H-24b), 1.05 (3H, s, H-29), 1.04 (3H, s, H-28), 1.03 (3H, d, J = 6.5 Hz, H-21), 1.02 (3H, s, H-18), 0.91 (6H, d, J = 6.5 Hz, H-26, H-27); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 213.3 (C-3), 146.1 (C-5), 116.5 (C-6), 78.9 (C-1), 55.2 (C-17), 55.2 (C-14), 50.8 (C-4), 49.0 (C-8), 45.6 (C-2), 42.0 (C-13), 41.3 (C-9), 39.6 (C-10), 38.3 (C-24), 37.7 (C-22), 35.5 (C-20), 33.1 (C-12), 32.3 (C-15), 29.7 (C-16), 29.5 (C-7), 28.1 (C-25), 25.9 (C-28), 25.0 (C-29), 23.8 (C-23), 23.7 (C-18), 23.5 (C-21), 22.8 (C-26), 22.8 (C-27), 18.8 (C-11), 15.6 (C-19), 12.2 (C-30); FABMS *m/z* 443 $[M + H]^+$; HRFABMS *m/z* 443.3895 $[M + H]^+$ (calcd for $C_{30}H_{51}O_2$, 443.3889).

Cornusalterin L (12): white, amorphous powder; mp 140.5−141.5 °C; $[\alpha]_D^{25}$ −89.6 (*c* 0.45, $CHCl_3$); CD (MeOH) λ_{max} ($\Delta\varepsilon$) 294 (−24.7), 265 (+4.2), 258 (+3.7) nm; IR (KBr) ν_{max} 2969, 1739, 1706, 1657, 1370, 1216, 1031, 695 cm^{-1}; ^1H NMR data, see Table 1; ^{13}C NMR data, see Table 2; FABMS *m/z* 439 $[M + H]^+$; HRFABMS *m/z* 439.3576 $[M + H]^+$ (calcd for $C_{30}H_{47}O_2$, 439.3576).

Deoxyflindissone (13): white, amorphous powder; mp 143.0−144.0 °C; $[\alpha]_D^{25}$ −41.0 (*c* 0.60, $CHCl_3$); CD (MeOH) λ_{max} ($\Delta\varepsilon$) 294 (−27.2), 266 (+6.8), 259 (−4.5) nm; IR (KBr) ν_{max} 2967, 1706, 1657, 1462, 1380, 1057, 725 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 5.32 (1H, m, H-7), 5.21 (1H, br d, J = 9.0 Hz, H-24), 4.66 (1H, m, H-23), 4.01 (1H, dd, J = 7.5, 7.5 Hz, H-21a), 3.27 (1H, dd, J = 9.5, 7.5 Hz, H-21b), 2.76 (1H, ddd, J = 14.5, 14.5, 5.0 Hz, H-2β), 2.33 (1H, m, H-9α), 2.25 (1H, ddd, J = 14.5, 5.0, 5.0 Hz, H-2α), 2.11 (1H, m, H-6a), 2.09

(1H, m, H-6b), 2.01 (1H, m, H-1β), 1.87 (1H, m, H-16β), 1.83 (1H, m, H-20), 1.78 (1H, m, H-15β), 1.77 (1H, m, H-22a), 1.75 (1H, m, H-5α), 1.73 (3H, s, H-27), 1.70 (3H, s, H-26), 1.66 (1H, m, H-22b), 1.60 (1H, m, H-11α), 1.58 (1H, m, H-12β), 1.51 (1H, m, H-15α), 1.50 (1H, m, H-12α), 1.48 (1H, m, H-16α), 1.45 (1H, m, H-1α), 1.44 (1H, m, H-17), 1.27 (1H, m, H-11β), 1.13 (3H, s, H-29), 1.06 (3H, s, H-28), 1.03 (6H, s, H-19, H-30), 0.85 (3H, s, H-18); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 216.7 (C-3), 145.5 (C-8), 134.9 (C-25), 126.8 (C-24), 118.1 (C-7), 75.7 (C-23), 73.5 (C-21), 52.4 (C-5), 50.5 (C-14), 50.4 (C-17), 48.4 (C-9), 47.8 (C-4), 43.9 (C-13), 42.1 (C-20), 38.4 (C-1), 37.3 (C-22), 35.1 (C-10), 34.9 (C-2), 34.3 (C-15), 32.3 (C-12), 27.4 (C-16), 27.2 (C-30), 25.7 (C-27), 24.5 (C-28), 24.3 (C-6), 22.6 (C-18), 21.5 (C-29), 18.0 (C-26), 17.8 (C-11), 12.7 (C-19); FABMS *m/z* 439 $[M + H]^+$.

(−)-Leucophyllone (14): white, amorphous powder; mp 123.0−124.0 °C; $[\alpha]_D^{25}$ −102.3 (*c* 0.93, $CHCl_3$); CD (MeOH) λ_{max} ($\Delta\varepsilon$) 295 (−19.5), 255 (+6.6) nm; IR (KBr) ν_{max} 2948, 1708, 1657, 1373, 1031, 727 cm^{-1}; FABMS *m/z* 455 $[M + H]^+$; ^{1}H and ^{13}C NMR data were identical to reported data.[12]

Demethylation of Compounds 7 and 9 (ref 18). To 4.5 mg of compound **7** in an NMR tube was added 0.5 mL of $CDCl_3$ to give a clear solution. Then 0.1 mL of trimethylsilyl iodide was added. The solution was maintained at room temperature, and the reaction was monitored by NMR periodically. The reaction was apparently complete after 24 h, as indicated by the absence of a signal for the OCH_3 protons in the NMR spectrum and the presence of a signal at δ 2.09 for protons of CH_3I. The brown-purple solution was filtered, and 0.5 mL of MeOH was added to the filtrate. After 2 h, the solvent was evaporated under vacuum to give a brown gum (6.0 mg), which was suspended in H_2O (3 mL) and partitioned with $CHCl_3$ to yield a purple extract (5.5 mg). The extract was further purified by a silica gel Waters Sep-Pak Vac 6 cc using a solvent system of *n*-hexane−EtOAc (10:1) to give **7a** (4.0 mg), 3-oxotirucalla-7,24-dien-23-ol. Compound **9** (4.0 mg) was also reacted with trimethylsilyl iodide as described above to afford **9a** (3.5 mg), 3-oxotirucalla-7,9,24-trien-23-ol.

7a: colorless gum; $[\alpha]_D^{25}$ −45.6 (*c* 0.20, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.34 (1H, m, H-7), 5.17 (1H, br d, J = 9.0 Hz, H-24), 4.34 (1H, ddd, J = 9.0, 9.0, 2.0 Hz, H-23), 2.75 (1H, ddd, J = 14.5, 14.5, 5.0 Hz, H-2β), 2.24 (1H, ddd, J = 14.5, 5.0, 5.0 Hz, H-2α), 1.76 (3H, s, H-27), 1.71 (3H, s, H-26), 1.70 (1H, m, H-20), 1.12 (3H, s, H-29), 1.06 (3H, s, H-28), 1.02 (3H, s, H-30), 1.01 (3H, s, H-19), 0.97 (3H, d, J = 6.0 Hz, H-21), 0.83 (3H, s, H-18); FABMS *m/z* 441 $[M + H]^+$.

9a: colorless gum; $[\alpha]_D^{25}$ −21.8 (*c* 0.17, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.41 (1H, m, H-11), 5.29 (1H, m, H-7), 5.10 (1H, br d, J = 10.0 Hz, H-24), 4.33 (1H, ddd, J = 10.0, 10.0, 4.0 Hz, H-23), 2.74 (1H, ddd, J = 14.5, 14.5, 5.0 Hz, H-2β), 2.25 (1H, ddd, J = 14.5, 5.0, 5.0 Hz, H-2α), 1.77 (3H, s, H-27), 1.72 (3H, s, H-26), 1.70 (1H, m, H-20), 1.11 (3H, s, H-29), 1.06 (3H, s, H-28), 1.02 (3H, s, H-30), 1.01 (3H, s, H-19), 0.95 (3H, d, J = 6.0 Hz, H-21), 0.81 (3H, s, H-18); FABMS *m/z* 439 $[M + H]^+$.

Preparation of the (*R*)- and (*S*)-MTPA Ester Derivatives of Compounds 7a and 9a (ref 19). To a stirred solution of **7a** (2.0 mg) in pyridine (400 μL) were added 4-(dimethylamino)pyridine (2 mg) and (*S*)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (MTPA-Cl, 10 μL). The mixture was stirred at room temperature for 16 h. The reaction mixture was then passed through a silica gel Waters Sep-Pak Vac 6 cc and eluted with *n*-hexane−EtOAc (15:1) to give the respective (*R*)-Mosher ester **7r**. Treatment of **7a** (2.0 mg) with (*R*)-MTPA-Cl (10 μL) as described above yielded the corresponding (*S*)-MTPA ester **7s**. Similarly, treatment of **9a** with (*S*)- and (*R*)-MTPA-Cl afforded the respective Mosher esters **9r** and **9s**.

In Vitro Cytotoxicity Test. A sulforhodamine B (SRB) bioassay was used to determine the cytotoxicity of each compound against four cultured human cancer cell lines.[21] The assays were performed at the Korea Research Institute of Chemical Technology. The cell lines used were A549 (non small cell lung adenocarcinoma), SK-OV-3 (ovarian cancer cells), SK-MEL-2 (skin melanoma), and XF498 (human CNS cancer). Etoposide was used as a positive control. The cytotoxicities of etoposide against the A549, SK-OV-3, SK-MEL-2, and XF498 cell lines were IC_{50} 1.85, 1.81, 1.17, and 1.72 μM, respectively.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra for **1**−**13**, 2D NMR (HMQC, HMBC, NOESY) data for **4**−**7** and **11**−**13**, CD spectrum for **1**, **7**, and **12**−**14**, HMBC correlations for **1**−**2**, **4**−**7**, and **9**−**12**, NOESY correlations for **1**, **5**, **7**, **8**, and **11**−**13**, partial ^{1}H NMR data of the (*S*)- and (*R*)-MTPA esters of **7a** and **9a**, and cytotoxic activities of compounds **1**−**14**. This material is available free of charge via the Internet at http://pubs.acs.org.

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