Four New Nortriterpenoids from *Schisandra lancifolia*

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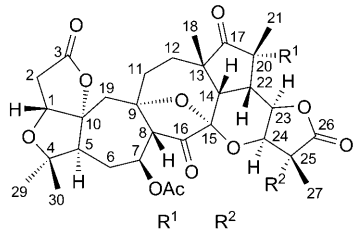
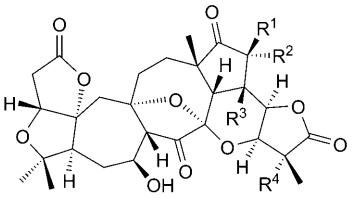
Four new highly oxygenated nortriterpenoids, lancifodilactones O–R (**1**–**4**), together with six known ones, *i.e.*, **5**–**10**, were isolated from the leaves and stems of *Schisandra lancifolia*. Their structures were elucidated by spectroscopic analyses, including 1D- and 2D-NMR experiments and mass spectrometry. Compounds **1**–**3** were evaluated for their cytotoxicity against NB4, A549, SHSY5Y, PC-3, and MCF-7 cell lines. No compounds exhibited significant cytotoxicity, the IC_{50} values being above 50 μM.

Introduction. – The genus *Schisandra* of the family Schisandraceae is economically and medicinally valuable and is widely used in traditional Chinese medicine. They are rich sources of bioactive lignans, which possess various beneficial pharmacological effects such as antihepatitis, antitumor, and anti-HIV-1 activity [1–6]. Recent research by our group on *Schisandra* species has resulted in the characterization of a series of structurally interesting secondary metabolites endowed with different oxygenated skeletons, which may be grouped into schiartane, 18-norschiartane, 18(13 → 14)-*abeo*-schiartane, schisanartane, pre-schisanartane, and wuweiziartane types [7]. Some of them exhibited modest or strong anti-HIV activities [8–10] and cytotoxicity [11–12].

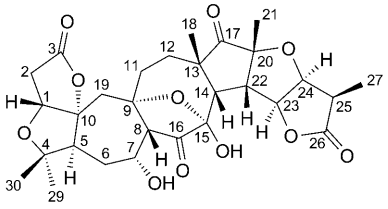
Schisandra lancifolia (REHD. et WILS) A. C. SMITH is a climbing plant mainly distributed in the mainland of China. Our previous research on this plant collected from the Yunnan region of China led to the discovery of some new highly oxygenated nortriterpenoids [9–10][13–17]. As part of our continuing work to discover additional novel compounds from the *Schisandra* genus, the leaves and stems of *S. lancifolia* growing in the Sichuan region of China were collected for our present phytochemical research and led to the isolation of four new minor nortriterpenoids, lancifodilactones O–R (**1**–**4**), together with six known ones including lancifodilactones C and D (**5** and **6**) [15], micrandilactone A (**7**) [18], micrandilactones D and F (**8** and **9**) [19], and lancifodilactone L (**10**) [13]. The structures of **1**–**4** were determined by extensive NMR spectroscopic experiments, including ^{1}H,^{1}H-COSY, HSQC, HMBC, and ROESY techniques. In addition, the new compounds **1**–**3** were evaluated for cytotoxicity against NB4, A549, SHSY5Y, PC-3, and MCF-7 cell lines. The present article reports the isolation, structural elucidation, and biological evaluation of the new compounds.



	R^1	R^2
1	H	OH
2	OH	H
3	H	H



	R^1	R^2	R^3	R^4
5	H	Me	H	H
7	Me	OH	OH	H
8	Me	OH	H	H
10	Me	H	H	OH



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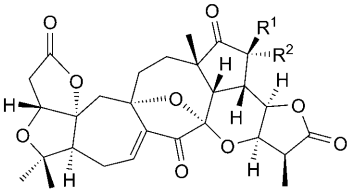


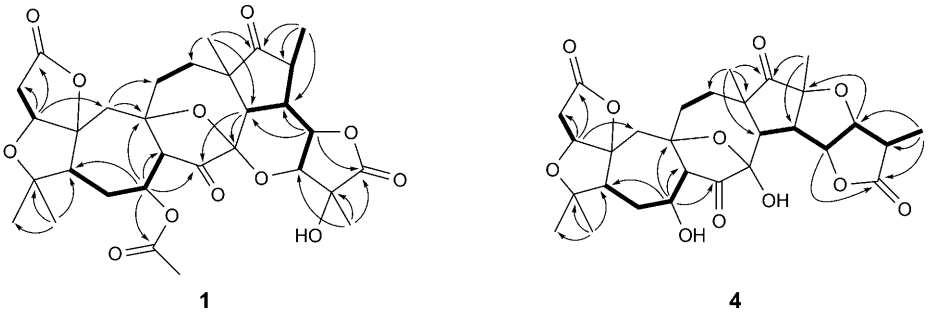
	R^1	R^2
6	Me	H
9	OH	Me

Results and Discussion. – Lancifodilactone O (**1**) gave a quasi-molecular-ion peak at *m/z* 625 ($[M+Na]^+$) in its positive-ion-mode ESI-MS and was assigned the molecular formula $C_{31}H_{38}O_{12}$, which was confirmed by HR-ESI-MS (*m/z* 625.2360 ($[M+Na]^+$) and NMR data. Obvious in the ^{1}H-NMR spectrum were six Me signals due to five tertiary Me and a secondary Me group. ^{1}H- and ^{13}C-NMR data revealed the presence of an Ac group (δ(C) 169.6 and 20.8; δ(H) 2.10). In addition, other signals for 29 C-atoms were observable in the ^{13}C- and DEPT-NMR spectra of **1**, including two ester groups, two ketone groups, six quaternary C-atoms (five oxygenated ones), and nine CH (four oxygenated ones), five CH_2, and five Me groups. This suggested that compound **1** was a highly oxygenated nortriterpene containing seven rings. Analysis of the ^{13}C- and ^{1}H-NMR data of **1** (*Tables 1* and *2*) revealed that they are similar to those reported for lancifodilactone L (**10**) [13], which was also isolated in our present studies. Comparison of 1D-NMR data, together with detailed HMBC and ^{1}H,^{1}H-COSY analyses (*Fig. 1*) indicated that the difference was an additional Ac group in **1**. A HMBC of the signal at H–C(7) with the C=O C-atom of the Ac group indicated that the Ac group was located at C(7) (*Fig. 1*). The downfield chemical shift of H–C(7) from δ(H) 4.56 in **10** [13] to δ(H) 5.68–5.73 in **1** also supported the above deduction. Therefore, the constitution of **1** was established.

The relative configuration of **1** was established by chemical-shift comparison with those of **10** and analysis of its ROESY NMR data (*Fig. 2*). Biogenetically, H–C(5) should be α- and Me(18) β-oriented [19]. H–C(5) showed a ROESY correlation with H–C(7), indicating α-orientation of H–C(7). Accordingly, the Ac group was assigned as being β-oriented. ROESY Correlations of Me(18) with H–C(14), H–C(22), and Me(21) indicated that H–C(14), H–C(22), and Me(21) were all β-oriented. In

Table 1. *^{13}C-NMR Data* (C_5D_5N) *of Compounds* **1**–**4**. δ in ppm.

	1	**2**	**3**	**4**		**1**	**2**	**3**	**4**
C(1)	81.5 (*d*)	81.6 (*d*)	81.5 (*d*)	81.8 (*d*)	C(17)	220.2 (*s*)	220.1 (*s*)	220.4 (*s*)	219.5 (*s*)
C(2)	35.3 (*t*)	35.3 (*t*)	35.4 (*t*)	35.4 (*t*)	C(18)	25.8 (*q*)	26.7 (*q*)	25.9 (*q*)	28.2 (*q*)
C(3)	175.4 (*s*)	175.3 (*s*)	175.6 (*s*)	175.7 (*s*)	C(19)	42.5 (*t*)	42.3 (*t*)	42.1 (*t*)	43.6 (*t*)
C(4)	83.7 (*s*)	83.5 (*s*)	83.7 (*s*)	84.0 (*s*)	C(20)	40.2 (*d*)	75.0 (*s*)	44.7 (*d*)	88.1 (*s*)
C(5)	57.9 (*d*)	58.0 (*d*)	57.9 (*d*)	53.5 (*d*)	C(21)	14.9 (*q*)	24.6 (*q*)	15.0 (*q*)	25.1 (*q*)
C(6)	33.0 (*t*)	33.1 (*t*)	33.0 (*t*)	32.2 (*t*)	C(22)	44.5 (*d*)	41.3 (*d*)	40.2 (*d*)	51.7 (*d*)
C(7)	69.3 (*d*)	69.6 (*d*)	69.4 (*d*)	63.9 (*d*)	C(23)	73.4 (*d*)	73.8 (*d*)	75.2 (*d*)	87.9 (*d*)
C(8)	55.6 (*d*)	55.8 (*d*)	55.6 (*d*)	57.0 (*d*)	C(24)	74.8 (*d*)	72.5 (*d*)	69.2 (*d*)	84.7 (*d*)
C(9)	81.1 (*s*)	81.5 (*s*)	81.0 (*s*)	79.9 (*s*)	C(25)	76.9 (*s*)	42.0 (*d*)	42.4 (*d*)	42.7 (*d*)
C(10)	95.5 (*s*)	95.7 (*s*)	95.6 (*s*)	96.4 (*s*)	C(26)	177.5 (*s*)	177.9 (*s*)	178.0 (*s*)	178.7 (*s*)
C(11)	41.5 (*t*)	41.3 (*t*)	41.5 (*t*)	37.0 (*t*)	C(27)	17.8 (*q*)	8.0 (*q*)	8.2 (*q*)	9.7 (*q*)
C(12)	30.9 (*t*)	30.4 (*t*)	30.1 (*t*)	31.3 (*t*)	C(29)	27.6 (*q*)	27.8 (*q*)	27.6 (*q*)	21.5 (*q*)
C(13)	50.0 (*s*)	49.8 (*s*)	50.1 (*s*)	50.4 (*s*)	C(30)	20.8 (*q*)	20.6 (*q*)	20.8 (*q*)	29.4 (*q*)
C(14)	44.8 (*d*)	44.6 (*d*)	44.8 (*d*)	51.3 (*d*)	AcO	20.8 (*q*),	20.8 (*q*),	20.9 (*q*),	
C(15)	99.0 (*s*)	98.5 (*s*)	98.8 (*s*)	100.1 (*s*)		169.6 (*s*)	169.5 (*s*)	169.6 (*s*)	
C(16)	208.2 (*s*)	208.3 (*s*)	208.2 (*s*)	214.0 (*s*)					



1 **4**

Fig. 1. *Selected 2D-NMR correlations of compounds* **1** *and* **4**. Bond in bold indicates ^{1}H,^{1}H-COSY, arrow indicates HMBC.

addition, ROESY correlations of Me(27) with H–C(14) and H–C(22) indicated that Me(27) was also β-oriented and that, therefore, OH–C(25) was α-oriented.

In addition, a computer-generated 3D structure of **1** was obtained by CHEM 3D ULTRA V 8.0, with MM2 force-field calculations for energy minimization (*Fig. 2*). The calculated interatomic distances between the H-atom pairs H–C(5)/H–C(7) (2.33 Å), H–C(1)/Me(30) (2.58 Å), Me(18)/H–C(14) (2.64 Å), Me(18)/H–C(22) (2.64 Å), Me(18)/Me(21) (3.60 Å), H–C(14)/Me(27) (2.59 Å), and H–C(22)/Me(27) (2.44 Å) are all less than 4.00 Å; this further supported the well-defined ROESY correlations observed for each of these H-atom pairs.

Lancifodilactone P (**2**) was obtained as an optically active white powder. HR-ESI-MS Analysis of **2** showed that it has the same molecular formula $C_{31}H_{38}O_{12}$ as **1**. The ^{1}H- and ^{13}C-NMR data of **2** were very similar to those of **1**. A side-by-side comparison

Table 2. *^{1}H-NMR Data* (C_5D_5N) *of Compounds* **1**–**4**. δ in ppm, J in Hz.

	1	**2**	**3**	**4**
H–C(1)	4.27 (*d*, *J* = 4.6)	4.22 (*d*, *J* = 4.7)	4.25 (*d*, *J* = 4.8)	4.24 (*d*, *J* = 5.1)
CH_2(2)	2.75 (*d*, *J* = 16.5, H_α), 3.10 (*dd*, *J* = 4.6, 16.5, H_β)	2.83 (*d*, *J* = 16.0, H_α), 3.01 (*dd*, *J* = 4.7, 16.0, H_β)	2.80 (*d*, *J* = 16.1, H_α), 3.09 (*dd*, *J* = 4.8, 16.1, H_β)	2.84 (*d*, *J* = 15.4, H_α), 3.09 (*dd*, *J* = 5.1, 15.4, H_β)
H-C(5)	2.65 (*dd*, *J* = 4.1, 13.5)	2.65 (*dd*, *J* = 4.0, 13.6)	2.60 (*dd*, *J* = 4.1, 13.8)	2.85 (br. *d*, *J* = 10.1)
CH_2(6)	1.97–2.02 (H_α)[a]), 1.98–2.05 (H_β)[a])	1.98–2.05 (H_α)[a]), 2.03–2.08 (H_β)[a])	1.98–2.02 (H_α)[a]), 2.00–2.05 (H_β)[a])	1.82–1.86 (*m*, H_α), 1.54–1.60 (*m*, H_β)
H–C(7)	5.68–5.73 (*m*)	5.61–5.66 (*m*)	5.59–5.64 (*m*)	4.85–4.90 (*m*)
H–C(8)	3.03 (*d*, *J* = 13.5)	3.04 (*d*, *J* = 13.4)	3.05 (*d*, *J* = 13.4)	4.10 (*d*, *J* = 7.7)
CH_2(11)	2.00–2.05 (H_α)[a]), 1.69–1.74 (*m*, H_β)	2.04–2.08 (H_α)[a]), 1.67–1.72 (*m*, H_β)	2.08–2.13 (*m*, H_α), 1.65–1.75 (*m*, H_β)	1.97–2.02 (*m*, H_α), 1.63–1.67 (*m*, H_β)
CH_2(12)	1.87–1.92 (*m*, H_α), 1.48–1.52 (*m*, H_β)	1.83–1.90 (*m*, H_α), 1.53–1.58 (*m*, H_β)	1.84–1.90 (*m*, H_α), 1.50–1.56 (*m*, H_β)	2.03–2.08 (*m*, H_α), 1.67–1.72 (*m*, H_β)
H–C(14)	2.78 (*d*, *J* = 7.3)	2.87 (*d*, *J* = 6.8)	2.82 (*d*, *J* = 7.2)	3.52 (*d*, *J* = 10.7)
Me(18)	0.90 (*s*)	0.98 (*s*)	0.87 (*s*)	1.07 (*s*)
CH_2(19)	2.35 (*AB d*, *J* = 17.5, H_α), 2.45 (*AB d*, *J* = 17.5, H_β)	2.32 (*AB d*, *J* = 17.3, H_α), 2.50 (*AB d*, *J* = 17.3, H_β)	2.35 (*AB d*, *J* = 17.6, H_α), 2.48 (*AB d*, *J* = 17.6, H_β)	1.95 (*AB d*, *J* = 13.5, H_α), 2.51 (*AB d*, *J* = 13.5, H_β)
H–C(20)	2.88–2.93 (*m*)		2.85–2.91 (*m*)	
Me(21)	1.02 (*d*, *J* = 7.0)	1.54 (*s*)	1.10 (*s*)	1.53 (*s*)
H–C(22)	2.64–2.68 (*m*)	3.11–3.16 (*m*)	2.76–2.80 (*m*)	3.51 (*d*, *J* = 10.7)
H–C(23)	5.24 (br. *s*)	4.90 (br. *s*)	4.65 (br. *s*)	6.87 (*d*, *J* = 3.0)
H–C(24)	4.30 (br. *s*)	5.33 (br. *s*)	5.31 (br. *s*)	5.45 (br. *s*)
H–C(25)		3.19–3.24 (*m*)	3.22–3.27 (*m*)	3.28–3.33 (*m*)
Me(27)	2.07 (*s*)	2.01 (*d*, *J* = 6.8)	1.56 (*d*, *J* = 7.2)	1.44 (*d*, *J* = 7.3)
Me(29)	1.04 (*s*)	1.02 (*s*)	1.00 (*s*)	1.02 (*s*)
Me(30)	1.18 (*s*)	1.21 (*s*)	1.17 (*s*)	1.17 (*s*)
AcO	2.10 (*s*)	2.08 (*s*)	2.09 (*s*)	

[a]) Overlapped.

of the 1D-NMR data of **2** and **1** showed that the differences were due to the position change of an OH group from C(25) in **1** to C(20) in **2**. This was confirmed by HMBCs from Me(21) (δ(H) 1.54 (*s*)) to C(20) (δ(C) 75.5), C(22) (δ(C) 41.3), and C(17) (δ(C) 220.1). In addition, the ROESY correlations Me(18)/Me(21), Me(27)/H–C(14), and H–C(25)/H–C(23) indicated that both Me(21) and Me(27) were β-oriented. Accordingly, OH–C(20) was α-oriented.

The composition of lancifodilactone Q (**3**) was found to be $C_{31}H_{38}O_{11}$ by HR-ESI-MS (*m*/*z* 609.2408 ($[M+Na]^+$)), corresponding to 16 mass units less than **1**. Observed in the ^{1}H-NMR spectrum were six Me signals due to four tertiary Me and two secondary Me groups. 1D-NMR Data showed the presence of an Ac group (δ(C) 169.6 and 20.9; δ(H) 2.09) and 29 C-atom signals belonging to a nortriterpene skeleton (*Tables 1* and *2*). Comparison of the 1D-NMR data of **3** with those of **1** showed that the difference was that the oxygenated quaternary C(25) of **1** was replaced by a CH group

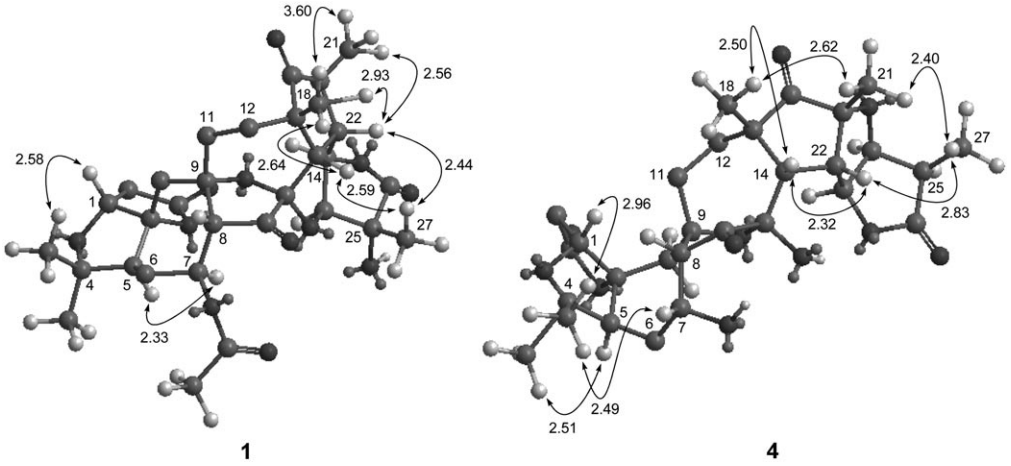


Fig. 2. *Key ROESY correlations of* **1** *and* **4** *and corresponding interatomic distances* [Å]. Some H-atoms are hidden for concision of the picture.

in **3**. This was confirmed by HMBCs from Me(27) (δ(H) 1.56 (*d*, $J = 7.2$ Hz) to C(24) (δ(C) 69.2), C(25) (δ(C) 42.4), and C(26) (δ(C) 178.0). The ROESY correlations H−C(25)/H−C(23) showed that H−C(25) was α-oriented. The remaining relative configurations of **3** were deduced to be the same as those of **1** by analysis of a ROESY plot and comparisons of chemical-shift data with those of **1** (*Table 1*).

The molecular formula of lancifodilactone R (**4**) was deduced as $C_{29}H_{36}O_{11}$ from its HR-ESI-MS (*m*/*z* 583.2304 ($[M + Na]^+$)). The ^{1}H- and ^{13}C-NMR data were very close to those of rubrifloradilactone C. Analysis of ^{1}H,^{1}H-COSY and HMBC data (*Fig. 1*) showed that **4** possessed the same planar structure as rubrifloradilactone C [11]. The significant chemical-shift differences observed in the NMR spectra between **4** and rubrifloradilactone C were associated with the signals at C(5)−C(8) and C(11). The HMBCs H−C(5)/C(7), and H−C(7)/C(5), C(8), C(9), and C(16), and the ^{1}H,^{1}H-COSYs H−C(5)/H−C(6)/H−C(7)/H−C(8) fully corroborated that the OH group was also located at C(7) in **4**. This suggested that the differences between **4** and rubrifloradilactone C were the relative configurations in the C(5) to C(8) region. A ROESY correlation (*Fig. 2*) between Me(29) and H−C(5) established that the configuration at C(5) was the same in both compounds. The coupling constant between H−C(7) and H−C(8) of **4** ($J = 7.7$ Hz) was much smaller than that in rubrifloradilactone C ($J = 10.2$ Hz), indicating that OH−C(7) may be α-oriented in **4**, opposed to that in rubrifloradilactone C. This deduction was supported by the downfield chemical shift of H−C(5) from δ(H) 2.35 in rubrifloradilactone C to δ(H) 2.85 in **4** due to the deshielding effect by the α-positioned OH−C(7) in **4**, and by the HMBC Me(30)/H−C(7). In addition, the absence of a ROESY correlation H−C(5)/H−C(7) also supported the above deduction. Other chiral centers of **4** were established to have the same relative configuration as those of rubrifloradilactone C by comparison of their 1D-NMR data and by the observed ROESY correlation of **4** (*Fig. 2*). Therefore, the structure of **4** was established.

The new compounds **1**–**3** were screened for their cytotoxicity against NB4 (acute promyelocytic leukemia), A549 (lung cancer), SHSY5Y (neuroblastoma), PC-3 (prostate cancer), MCF-7 (breast cancer) cell lines, by using taxol as positive control [20]. None of the tested compounds showed any significant cytotoxicity against the cell lines, the IC_{50} values being above 50 μM. Compound **4** was not tested for its bioactivity due to the limited amount available.

This project was supported financially by the *NSFC* (No. 30830115 and 20802082), projects from the Chinese Academy of Sciences ('*Xibuzhiguang*' to *W.-L. X.* and No. KSCX1-YW-R-24), the *973 Program* (No. 2009CB522300 and 2009CB940900), and the *Young Academic and Technical Leader Rising Foundation of Yunnan Province* (2006PY01-47).

Experimental Part

General. Column chromatography (CC): silica gel (SiO_2; 200–300 mesh, *Qingdao Marine Chemical Inc.*, Qingdao, China). Prep. HPLC: *Agilent-1100* liquid chromatograph; *Zorbax-SB-C*$_{18}$ column (9.4 mm × 25 cm). TLC: visualization by heating the SiO_2 plates sprayed with 10% H_2SO_4 in EtOH. M.p.: *XRC-1* micro melting point apparatus; uncorrected. Optical rotations: *Horiba-SEPA-300* polarimeter. UV Spectra: *Shimadzu-UV-2401A* spectrophotometer; λ_{max} (log ε) in nm. IR Spectra: *Bruker-Tensor-27* spectrophotometer, KBr pellets; $\tilde{\nu}$ in cm^{-1}. 1D- and 2D-NMR Spectra: *Bruker-AM-400* and *-DRX-500* spectrometers; δ in ppm rel. to solvent signals, *J* in Hz. MS: *VG-Autospec-3000* spectrometer; at 70 eV; in *m*/*z* (rel. %).

Plant Material. The stems of *S. lancifolia* were collected in the Erlang Mountain area of Sichuan Province, P. R. China., in September 2007. The identification of the plant material was verified by Prof. *Xi-Wen Li*. A voucher specimen (KIB-07-09-28) has been deposited with the State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, P. R. China.

Extraction and Isolation. The air-dried leaves and stems of *S. lancifolia* (3.2 kg) were powdered and extracted with 70% aq. actone (4 × 3.5 l) at r.t. The extract was filtered, the filtrate concentrated, and the obtained residue extracted with AcOEt. The AcOEt part (158 g) was subjected to CC (SiO_2, $CHCl_3$/MeOH gradient 20:1, 9:1, 8:2, 7:3, 6:4, and 5:5): *Fractions I–V. Fr. II* (20.4 g) was repeatedly subjected to CC (SiO_2 (200–300 mesh) and *Sephadex LH-20*); then the fractions were purified by prep. HPLC (MeOH/H_2O 45:55 and 40:60): **1** (5 mg), **3** (7 mg), **4** (2 mg), **7** (9 mg), and **8** (15 mg). *Fr. III* (16.5 g) was subjected to CC (SiO_2, $CHCl_3$/actone 10:1, 5:1, 2:1, and 1:1): *Frs. III-1–III-4. Fr. III-1* (2.8 g) was repeatedly subjected to CC (SiO_2, *RP-18*, and *Sephadex LH-20* (MeOH); then the fractions were purified by prep. HPLC (MeOH/MeCN/H_2O 20:25:55): **2** (6 mg), **5** (7 mg), and **9** (10 mg). Similarly, *Fr. III-2* (1.5 g) was subjected to chromatography methods mentioned above: **6** (7 mg) and **10** (15 mg).

Lancifodilactone O (= rel-*(1*R,*3a*R,*3b*S,*4*S,*5a*S,*7a*S,*8a*R,*11a*R,*13a*S,*15*S,*15a*R,*16a*S,*16b*S,*17a*S*)-15-(Acetyloxy)tetradecahydro-1-hydroxy-1,4,5a,13,13-pentamethyl-2*H,*8*H-*7a,16a-epoxy-10*H-*3,9,12,17-tetraoxacyclopent[3′,3′a]azuleno[6′,5′:5,6]cyclooct[1,2,3-*cd*]-as-*indacene-2,5,10,16(1*H,*13*H*)-tetrone*; **1**): White crystals. M.p. 173–174°. $[\alpha]_D^{25.5} = +80.7$ ($c = 0.10$, MeOH). UV (MeOH): 203 (3.25). IR: 3055, 2925, 2877, 1771, 1726, 1622, 1460, 1167, 1075, 1021, 879. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. ESI-MS (pos.): 625 ($[M+Na]^+$). HR-ESI-MS: 625.2360 ($[M+Na]^+$, $C_{31}H_{38}NaO_{12}^+$; calc. 625.2363).

Lancifodilactone P (= rel-*(1*R,*3a*S,*3b*R,*4*S,*5a*R,*7a*R,*8a*S,*11a*S,*13a*R,*15*R,*15a*S,*16a*R,*16b*R,*17a*S*)-15-(Acetyloxy)tetradecahydro-4-hydroxy-1,4,5a,13,13-pentamethyl-2*H,*8*H-*7a,16a-epoxy-10*H-*3,9,12,17-tetraoxacyclopent[3′,3′a]azuleno[6′,5′:5,6]cyclooct[1,2,3-*cd*]-as-*indacene-2,5,10,16(1*H,*13*H*)-tetrone*; **2**): White powder. $[\alpha]_D^{25.2} = +70.1$ ($c = 0.11$, MeOH). UV (MeOH): 202 (3.25). IR: 3417, 2915, 2856, 1761, 1632, 1373, 1120, 1019, 588. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. ESI-MS (pos.): 625 ($[M+Na]^+$). HR-ESI-MS: 625.2354 ($[M+Na]^+$, $C_{31}H_{38}NaO_{12}^+$; calc. 625.2363).

Lancifodilactone Q (= rel-*(1*R,*3a*S,*3b*R,*4*R,*5a*R,*7a*R,*8a*S,*11a*S,*13a*R,*15*R,*15a*S,*16a*R,*16b*R,*17a*S*)-15-(Acetyloxy)tetradecahydro-1,4,5a,13,13-pentamethyl-2*H,*8*H-*7a,16a-epoxy-10*H-*3,9,12,17-tetraoxacyclo-

pent[3′,3′a]azuleno[6′,5′:5,6]cyclooct[1,2,3-cd*]*-as-*indacene-2,5,10,16(1*H*,13*H*)-tetrone*; **3**): White powder. $[\alpha]_D^{24.7} = +68.3$ ($c = 0.15$, MeOH). UV (MeOH): 202 (3.31). IR: 2931, 1786, 1735, 1631, 1386, 1116, 1035, 1015, 589. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. ESI-MS (pos.): 609 ($[M+Na]^+$). HR-ESI-MS: 609.2408 ($[M+Na]^+$, $C_{31}H_{38}NaO_{11}^+$; calc. 609.2414).

Lancifodilactone R (= rel-*(3*R*,3a*S*,4a*R*,5a*S*,7a*S*,8a*R*,11a*R*,13a*S*,15*R*,15a*R*,17*S*,17a*S*,17b*S*,17c*S*)-Tetradecahydro-15,17-dihydroxy-3,4a,5a,13,13-pentamethyl-8*H*-7a,17-epoxy-10*H*-furo[3,2-*b*]furo[3‴′, 2‴′:2‴,3‴]furo[3‴,4‴:4″,5″]cyclohepta[1″,2″:5′,6′]cycloocta[1′,2′:4,5]cyclopenta[1,2-*d*]furan-2,5,10,16-(3*H*,7*H*,13*H*)-tetrone*; **4**): White powder. $[\alpha]_D^{25.0} = +30.3$ ($c = 0.08$, MeOH). UV (MeOH): 204 (3.15). IR: 3445, 2973, 2932, 1765, 1636, 1457, 1377, 1171, 1105, 986. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. ESI-MS (pos.): 583 ($[M+Na]^+$). HR-ESI-MS: 583.2304 ($[M+Na]^+$, $C_{29}H_{36}NaO_{11}^+$; calc. 583.2307).

Cellular Proliferation Assay. Colorimetric assays were performed to evaluate compound activity. The NB4 acute promyelocytic leukemia, the A549 lung cancer, the PC-3 prostate cancer, the MCF-7 breast cancer, and the SHSY5Y neuroblastoma cell line were treated with various concentrations of compounds (0, 0.01, 0.1, 1, 10, and 50 μM) in 96-well culture plates for 48 h in 200 μl of media and pulsed by addition of 10 μl of 2-(2-methoxy-4-nitrophenyl)-3-(4-nitrophenyl)-5-(2,4-disulfophenyl)-2*H*-tetrazolium (= WST-8; *Cell Counting Kit-8* from *Dojindo*, Kumamoto, Japan) to each well for 4 h. WST-8 is converted to WST-8-formazan upon bioreduction in the presence of the electron carrier 1-methoxy-5-methylphenazinium methyl sulfate that is abundant in viable cells. Absorbance readings at a wavelength of 450 nm were taken on a spectrophotometer (*Multiskan MK3*, *Thermo Lab Systems*). The concentration resulting in 50% of cell-growth inhibition (IC_{50}) was calculated with the Probit program in SPSS 7.5 for *Windows* 98 (*SPSS Inc.*, Chicago). Taxol was used as pos. control [20].

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Received January 5, 2010