New Xenicane Diterpenoids from the Gorgonian *Acalycigorgia inermis*

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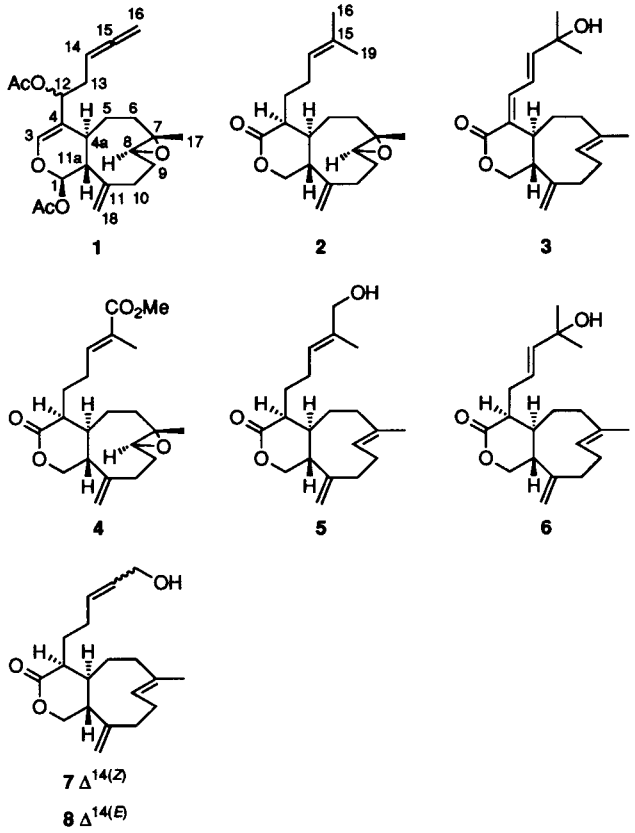
Eight diterpenes and norditerpenes including five new xenicane metabolites (**4**−**8**) have been isolated from the gorgonian *Acalycigorgia inermis*. The structures of these compounds have been determined by combined spectroscopic analysis. The new compounds exhibited significant cytotoxicity against a human leukemia cell-line.

Diterpenoids of the xenicane and related carbon skeletal classes have been frequently encountered in coelenterates of the orders Gorgonacea (gorgonians) and Alcyonacea (soft corals).[1,2] As part of our interest in exploring marine organisms for secondary metabolites, we reported the isolation and structure elucidation of acalycixeniolides D−G, cytotoxic diterpenes and norditerpenes of the xenicane class from the gorgonian *Acalycigorgia inermis* Hedlund (family Acanthogorgiidae) collected from the Keomun Island, Korea.[3] In our continuing search for bioactive agents from benthic invertebrates, we re-collected this animal from the nearby Bacdo. Guided by the cytotoxicity test and ^{1}H NMR analysis, the crude extract was separated utilizing chromatographic methods to yield several diterpenoids of the xenicane class. Herein we report the structures of five new and three known compounds. All of the new compounds exhibited significant cytotoxicity against the human leukemia cell-line K562. In addition, the bioactivity of acalycixeniolide E (**1**) was reevaluated.

On the basis of the combined spectroscopic analysis and comparison of the spectral data with previously reported data, the structures of compounds **1**−**3** were identified as acalycixeniolide E (**1**), acalycixeniolide F (**2**), and 9-deoxyxeniolide A (**3**), respectively. Compounds **1** and **2** were previously isolated from *A. inermis* collected from the Keomun Island, Korea, while **3** was reported as a bioactive constituent of an unidentified soft coral *Xenia* sp. from the Philippines.[3,4]

Acalycixeniolide H (**4**) was isolated as a white amorphous solid, which analyzed for $C_{21}H_{30}O_5$ by combined HREIMS and ^{13}C NMR analysis. The spectral data of this compound were highly compatible with those obtained for other xenicanes. Moreover, careful examination of the NMR data revealed that **4** possessed the same tricyclic moiety as **2** (Table 1). However, the appearance of three downfield signals at δ 170.0 (C), 142.9 (CH), and 129.4 (C) in the ^{13}C NMR data indicated the presence of an α,β-unsaturated carbonyl group at the side chain. This interpretation was supported by a characteristic absorption band at 1710 cm^{-1} in the IR spectrum and an absorption maximum at 216 nm in the UV spectrum. A combination of ^{1}H COSY, TOCSY, HSQC, and HMBC experiments determined the locus of this functionality at C-14 of the side chain. The presence of a methyl ester functionality {δ_H 3.72 (3H, s), δ_C 52.3 and 170.0} was confirmed by a long-range HMBC correlation between the methyl ester proton singlet and the ester carbonyl resonance. The *E* configuration was assigned to the C-14 double bond on the basis of a NOE correlation between the allylic protons at C-13 and C-19 as well as the upfield shift of the C-19 methyl carbon at δ 12.6 in the ^{13}C NMR data.[5]



The relative stereochemistry of **4** was determined by a ROESY experiment. The H-17 methyl proton at δ 1.37 showed correlations with the H-5β, H-9β, and H-11a protons at δ 1.07, 1.48, and 2.40, respectively. On the other hand, the H-8 epoxide proton at δ 2.94 showed strong cross-peaks with the H-4a and H-6α protons at δ 2.16 and 1.02, respectively. In addition, the H-4a proton exhibited mutual correlations with the H-4 and H-18 protons at δ 3.06 and 5.19, respectively. These results were identical to the previous ones based on the X-ray crystallographic analysis and NMR studies.[6,7] The relative configuration of the whole molecule was assigned as 4*S**,4a*S**,7*S**,8*S**,11a*R**.

The molecular formula of acalycixeniolide I (**5**) was deduced as $C_{20}H_{30}O_3$ by HREIMS analysis. The spectral data of this compound were similar to those of **4**. However,

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Table 1. ^{13}C NMR Assignments for Compounds **2** and **4**−**8**

position	**2**		**4**		**5**		**6**		**7**		**8**	
1	71.9	(t)	71.9	(t)	71.7	(t)	71.8	(t)	71.7	(t)	71.7	(t)
3	178.1	(s)	177.6	(s)	178.6	(s)	178.2	(s)	178.5	(s)	178.5	(s)
4	42.5	(d)	43.0	(d)	42.2	(d)	43.3	(d)	42.5	(d)	42.3	(d)
4a	45.5	(d)	45.9	(d)	45.9	(d)	45.3	(d)	46.7	(d)	46.1	(d)
5	29.6	(t)	29.7	(t)	31.2	(t)	30.8	(t)	31.3	(t)	31.2	(t)
6	40.8	(t)	40.7	(t)	40.9	(t)	40.6	(t)	40.9	(t)	40.9	(t)
7	60.9	(s)	60.8	(s)	136.9	(s)	136.9	(s)	136.8	(s)	136.8	(s)
8	63.5	(d)	63.5	(d)	125.2	(d)	125.1	(d)	125.2	(d)	125.2	(d)
9	26.3	(t)	26.4	(t)	26.0	(t)	26.0	(t)	26.0	(t)	26.0	(t)
10	34.3	(t)	34.3	(t)	36.5	(t)	36.6	(t)	36.5	(t)	36.5	(t)
11	152.4	(s)	152.2	(s)	154.4	(s)	154.5	(s)	154.4	(s)	154.4	(s)
11a	49.9	(d)	49.9	(d)	51.3	(d)	51.1	(d)	51.4	(d)	51.3	(d)
12	27.8	(t)	27.1	(t)	27.9	(t)	30.8	(t)	28.3	(t)	27.6	(t)
13	26.3	(t)	27.3	(t)	25.8	(t)	124.3	(d)	26.0	(t)	30.7	(t)
14	124.8	(d)	142.9	(d)	125.4	(d)	142.1	(d)	132.1	(d)	132.1	(d)
15	133.5	(s)	129.4	(s)	137.1	(s)	71.1	(s)	131.0	(d)	131.5	(d)
16	25.9	(q)	170.0	(s)	68.7	(t)	30.2	(q)[a]			63.5	(t)
17	16.4	(q)	16.4	(q)	16.6	(q)	16.6	(q)	16.6	(q)	16.6	(q)
18	114.5	(t)	114.6	(t)	113.1	(t)	113.0	(t)	113.2	(t)	113.2	(t)
19	17.9	(q)	12.6	(q)	13.9	(q)	30.0	(q)[a]	58.6	(t)		
OMe			52.3	(q)								

[a] Interchangeable signals.

signals of the C-16 methyl ester group of **4** in the ^1H and ^{13}C NMR data were replaced by those of a hydroxymethyl {δ_H 3.93 (2H, s), δ_C 68.7} in **5**. The molecular formula and chemical shift of the methylene group indicated the transformation of the methyl ester group to an allylic carbinol. This interpretation was confirmed by a combination of ^1H COSY, HSQC, and HMBC experiments as well as the characteristic absorption band of a hydroxyl group at 3400 cm^{-1} in the IR spectrum. The transformation of the C-7 epoxide group of **4** to a double bond in **5** was also determined by combined 2-D NMR analysis.

The molecular formula of acalycixeniolide J (**6**) was established as $C_{20}H_{30}O_3$ by HREIMS analysis. Although the spectral data of this compound were very similar to those of **5**, NMR signals corresponding to the side chain differed considerably. The most noticeable differences in the ^{13}C NMR data were the replacement of signals of C-13−C-16 at δ 25.8 (CH_2), 125.4 (CH), 137.1 (C), and 68.7 (CH_2) in **5** by those at δ 124.3 (CH), 142.1 (CH), 71.1 (C), and 30.2/30.0 (CH_3), respectively in **6** (Table 1). The corresponding change was also observed in the ^1H NMR data in which the signal of the H-16 oxymethylene at δ 3.93 (2H, s) was replaced by a methyl proton singlet at δ 1.27 (3H, s). In addition, the signal of a new olefinic proton appeared at δ 5.70 (1H, J = 15.6 Hz) in the ^1H NMR spectrum. These changes were accommodated by migration of the C-14 double bond and C-16 hydroxyl group to C-13 and C-15, respectively, which was confirmed by combined 2-D NMR experiments. The *E* geometry was assigned for the newly formed double bond on the basis of the large coupling constant (J = 15.6 Hz) between the olefinic protons.

Acalycixeniolides K (**7**) and L (**8**) were analyzed to have the identical molecular formula, $C_{19}H_{28}O_3$, by HREIMS and ^{13}C NMR spectrometry. The spectral data of these two compounds were very similar. A combination of 2-D NMR experiments showed that **7** and **8** possessed the same bicyclic moiety as **5** and **6**. The 2-D NMR data also revealed that both compounds had an allylic alcohol group at the terminus of the side chain. However, the structures of these compounds differ significantly from other xenicanes in losing a terminal methyl (or an equivalent) group, thus being norditerpenes.[7] Based upon the vicinal proton coupling constants ($J_{13,14}$ = 10.7 Hz for **7**)[8] and chemical shifts of the allylic carbons (δ 58.6 and 26.0 for **7**, δ 63.5 and 30.7 for **8**), the configurations at the C-13 double bond were assigned as *Z* and *E* for **7** and **8**, respectively.

Coelenterate-derived xenicane diterpeneoids and structurally related metabolites exhibit diverse bioactivities.[1] In our earlier investigation, acalycixeniolides D−G exhibited cytotoxicity in the range 0.2−56 μg/mL against the human leukemia cell-line K562.[3] In this study, 9-deoxyxeniolide A (**3**), previously reported to possess antibacterial activity, also exhibited potent cytotoxicity against the same cell-line with LC_{50} 0.04 μg/mL.[4] The newly isolated acalycixeniolides H−L (**4**−**8**) also showed cytotoxicity against K562 with LC_{50} values of 3.9, 1.2, 2.0, 1.8, and 1.5 μg/mL, respectively. In addition, acalycixeniolide E (**1**), a cyclic acetal derivative, exhibited 82% inhibitory activity against farnesyl protein transferase (FPT) at the concentration of 10 μg/mL. This compound was also found to have antiangiogenic activity, thus significantly inhibited tube-forming of the HUVEC (human umbilical vein endothelial cell) induced by bFGF (basic fibroblast growth factor) at the concentration of 10 μg/mL. However, other metabolites containing a lactone moiety instead of the cyclic acetal functionality of **1** were not active in both tests at the same or higher concentrations (up to of 20 μg/mL). Details of the antiangiogenic activity of acalycixeniolide E and its mode of action are currently under investigation and will be reported in due course.

Experimental Section

General Experimental Procedures. Melting points were measured on a Fisher-Johns apparatus and are uncorrected. Optical rotations were measured on a Jasco digital polarimeter using a 5 cm cell. IR spectra were recorded on a Mattson Galaxy spectrophotometer. UV spectra were obtained in methanol using a Milton-Roy spectrophotometer. NMR spectra were recorded in CD_3OD solutions on a Varian Unity 500 spectrometer. Proton and carbon NMR spectra were measured at 500 and 125 MHz, respectively. Chemical shifts are reported with respect to internal Me_4Si. Mass spectra were provided by Korea Basic Science Institute, Taejeon, Korea. All solvents used were spectral grade or were distilled prior to use.

Animal Material. *Acalycigorgia inermis* (sample number 980K-23) was collected by hand using scuba at 15−20 m depth in October 1998, at Bacdo, Korea. The collected samples were immediately frozen with dry ice and kept at −25 °C until chemically investigated. These animals had identical morpho-

logical characters including the color and branching pattern of the colony and the sizes of calyces with those identified previously (sample number 91K-4).[3] Furthermore, Si TLC analysis of the CH_2Cl_2 extracts from the randomly selected colonies (five from each collection) showed chemical homogeneity between specimens.

Extraction and Isolation. The animals (85 colonies, 4.5 kg) were defrosted, macerated, and repeatedly extracted with CH_2Cl_2 (9 L × 3) and MeOH (9 L × 2). The combined crude extracts (29.7 g) were partitioned between 15% aqueous MeOH and *n*-hexane. The aqueous MeOH layer was dried in vacuo (10.1 g) and subjected to C_{18} vacuum flash chromatography using stepped gradient mixtures of MeOH and H_2O as eluents (elution order: 50, 30, 20, 10% aqueous MeOH, and MeOH). The fraction eluted with 20% aqueous MeOH (1.56 g) was separated by semipreparative reversed-phase HPLC (YMC ODS-A column, 25% aqueous MeOH) to afford three peaks consisting mainly of xenicanes. The first fraction was purified by Si HPLC (YMC Si column, 30% EtOAc in *n*-hexane) to yield **4**. The second fraction was separated by Si HPLC (25% EtOAc in *n*-hexane) to yield **1**, **2**, **7**, and **8**. The third fraction was also separated under the same HPLC condition as the second one to yield **3**, **5**, and **6**. The amounts of pure materials were 9.8, 2.4, 29.8, 8.4, 14.6, 7.0, 7.0, and 10.2 mg for **1**−**8**, respectively.

Acalycixeniolide E (1): colorless gum, $[\alpha]^{25}_D$ 38.0° (*c* 0.12, MeOH); IR (KBr) ν_{max} 2930, 2860, 1955, 1740, 1660, 1370, 1150 cm^{-1}; LREIMS *m/z* $(M)^+$ *m/z* 402 ($C_{23}H_{30}O_6$).

Acalycixeniolide F (2): colorless gum, $[\alpha]^{25}_D$ 49.5° (*c* 0.15, MeOH); IR (KBr) ν_{max} 2930, 2860, 1955, 1740, 1640, 1540, 1370, 1150 cm^{-1}; LREIMS *m/z* $(M)^+$ *m/z* 318 ($C_{20}H_{30}O_3$).

9-Deoxyxeniolide A (3): amorphous solid; mp 124−126 °C; $[\alpha]^{25}_D$ 20.5° (*c* 0.12, MeOH); IR (KBr) ν_{max} 2930, 2860, 1710, 1630, 1370, 1230, 1145 cm^{-1}; UV (MeOH) λ_{max} (log ϵ) 268 (4.40) nm; HRDCIMS $(M + H)^+$ *m/z* obsd 317.2113; calcd for $C_{20}H_{29}O_3$, 317.2116 (Δ −0.3 mmu).

Acalycixeniolide H (4): amorphous solid; mp 162−164 °C; $[\alpha]^{25}_D$ 156.5° (*c* 0.11, MeOH); IR (KBr) ν_{max} 2950, 1745, 1710, 1645, 1435, 1390, 1265, 1130 cm^{-1}; UV (MeOH) λ_{max} (log ϵ) 216 (3.92) nm; ^{1}H NMR (CD_3OD) δ 6.78 (1H, ddq, *J* = 7.8, 7.3, 1.5 Hz, H-14), 5.19 (1H, s, H-18), 5.16 (1H, s, H-18), 4.31 (1H, dd, *J* = 11.7, 6.8 Hz, H-1), 4.08 (1H, t, *J* = 11.7 Hz, H-1), 3.72 (3H, s, OMe), 3.06 (1H, dt, *J* = 6.4, 6.8 Hz, H-4), 2.94 (1H, dd, *J* = 10.3, 4.4 Hz, H-8), 2.53 (1H, dt, *J* = 13.2, 2.9 Hz, H-10), 2.40 (1H, m, H-11a), 2.32 (1H, ddt, *J* = 14.2, 7.8, 6.4 Hz, H-13), 2.26 (1H, m, H-13), 2.24 (1H, m, H-9), 2.22 (1H, m, H-10), 2.19 (1H, m, H-6), 2.16 (1H, m, H-4a), 1.98 (1H, m, H-12), 1.84 (3H, d, *J* = 1.5 Hz, H-19), 1.77 (1H, br ddd, *J* = 13.7, 3.4, 2.9 Hz, H-5), 1.59 (1H, ddt, *J* = 14.2, 8.8, 6.4 Hz, H-12), 1.48 (1H, m, H-9), 1.37 (3H, s, H-17), 1.07 (1H, dddd, *J* = 13.7, 13.7, 10.7, 2.9 Hz, H-5), 1.02 (1H, dt, *J* = 3.4, 13.7 Hz, H-6); ^{13}C NMR data, see Table 1; HMBC correlations (7 Hz) H-1/C-3, C-4a, C-11, C-11a; H-4/C-3, C-4a, C-5, C-11a, C-12; H-5/C-4, C-4a, C-6, C-7; H-6/C-4a, C-5, C-7; H-8/C-6, C-7, C-9; H-9/C-8, C-10, C-11; H-10/C-8, C-9, C-11, C-11a, C-18; H-12/C-3, C-4, C-4a, C-13, C-14; H-13/C-4, C-12, C-14, C-15; H-14/C-13, C-15, C-16, C-19; H-17/C-6, C-7, C-8; H-18/C-1, C-10, C-11, C-11a; H-19/C-14, C-15, C-16; OMe/C-16; ROESY correlations H-1/H-4, H-1/H-18, H-4/H-4a, H-4/H-11, H-4/H-18, H-4a/H-8, H-4a/H-11, H-4a/H-18, H-5β(δ 1.07)/H-17, H-5β/H-11a, H-6α(δ 1.02)/H-8, H-9β(δ 1.48)/H-17, H-11a/H-17; HREIMS $(M)^+$ *m/z* obsd 362.2090; calcd for $C_{21}H_{30}O_5$, 362.2093 (Δ −0.3 mmu).

Acalycixeniolide I (5): amorphous solid; mp 95−98 °C; $[\alpha]^{25}_D$ 103.9° (*c* 0.35, MeOH); IR (KBr) ν_{max} 3400, 2930, 2860, 1740, 1640, 1450, 1390, 1140, 1025 cm^{-1}; ^{1}H NMR (CD_3OD) δ 5.43 (1H, t, *J* = 7.3 Hz, H-14), 5.37 (1H, t, *J* = 8.3 Hz, 8.3 Hz, H-8), 5.05 (1H, s, H-18), 4.98 (1H, s, H-18), 4.16 (1H, dd, *J* = 11.7, 6.8 Hz, H-1), 4.01 (1H, dd, *J* = 12.2, 11.7 Hz, H-1), 3.93 (2H, s, H-16), 3.02 (1H, dt, *J* = 6.4, 6.8 Hz, H-4), 2.49 (1H, ddd, *J* = 12.7, 10.3, 8.3 Hz, H-9), 2.33 (1H, dd, *J* = 12.2, 8.8 Hz, H-10), 2.19 (1H, ddd, *J* = 12.7, 3.4, 2.9 Hz, H-6), 2.17 (1H, m, H-10), 2.13 (3H, m, H-4a, H-13 (2H)), 2.06 (1H, m, H-9), 2.02 (1H, m, H-11a), 1.98 (1H, dt, *J* = 4.4, 12.7 Hz, H-6), 1.91 (1H, ddt, *J* = 13.6, 6.8, 7.3 Hz, H-12), 1.70 (3H, s, H-17), 1.67 (3H, s, H-19), 1.66 (1H, m, H-5), 1.55 (1H, ddt, *J* = 13.6, 6.4, 7.3 Hz, H-12), 1.02 (1H, dddd, *J* = 13.7, 13.2, 10.3, 3.4 Hz, H-5); ^{13}C NMR data, see Table 1; HRDCIMS $(M + NH_4)^+$ *m/z* obsd 336.2545; calcd for $C_{20}H_{34}NO_3$, 336.2539 (Δ −0.7 mmu).

Acalycixeniolide J (6): amorphous solid; mp 93−95 °C; $[\alpha]^{25}_D$ 49.4° (*c* 0.14, MeOH); IR (KBr) ν_{max} 3450, 2970, 2930, 1745, 1640, 1390, 1140 cm^{-1}; ^{1}H NMR (CD_3OD) δ 5.70 (1H, d, *J* = 15.6 Hz, H-14), 5.60 (1H, ddd, *J* = 15.6, 8.8, 5.4 Hz, H-13), 5.34 (1H, t, *J* = 8.3 Hz, H-8), 5.08 (1H, s, H-18), 4.99 (1H, s, H-18), 4.17 (1H, dd, *J* = 11.7, 6.8 Hz, H-1), 4.04 (1H, dd, *J* = 12.2, 11.7 Hz, H-1), 3.10 (1H, ddd, *J* = 8.3, 6.3, 5.9 Hz, H-4), 2.53 (1H, dddd, *J* = 14.2, 6.3, 5.4, 1.5 Hz, H-12), 2.49 (1H, ddd, *J* = 13.2, 9.3, 8.3 Hz, H-9), 2.33 (1H, dd, *J* = 12.2, 8.8 Hz, H-10), 2.22 (1H, ddd, *J* = 14.2, 8.8, 8.3 Hz, H-12), 2.18 (1H, m, H-10), 2.16 (1H, m, H-6), 2.13 (1H, m, H-4a), 2.03 (1H, m, H-9), 2.01 (1H, m, H-11a), 1.99 (1H, ddd, *J* = 13.2, 12.7, 3.9 Hz, H-6), 1.71 (1H, m, H-5), 1.70 (3H, s, H-17), 1.27 (3H, s, H-16), 1.26 (3H, s, H-19), 0.99 (1H, ddt, *J* = 10.8, 3.9, 13.2 Hz, H-5); ^{13}C NMR data, see Table 1; HREIMS $(M)^+$ *m/z* obsd 318.2196; calcd for $C_{20}H_{30}O_3$, 318.2195 (Δ 0.1 mmu).

Acalycixeniolide K (7): amorphous solid; mp 127−129 °C; $[\alpha]^{25}_D$ 36.8° (*c* 0.10, MeOH); IR (KBr) ν_{max} 3400, 2930, 1745, 1640, 1450, 1390, 1145, 1030 cm^{-1}; ^{1}H NMR (CD_3OD) δ 5.62 (1H, br dt, *J* = 10.7, 6.4 Hz, H-15), 5.53 (1H, br dt, *J* = 10.7, 7.3 Hz, H-14), 5.37 (1H, t, *J* = 7.8 Hz, H-8), 5.07 (1H, s, H-18), 5.00 (1H, s, H-18), 4.15 (1H, dd, *J* = 11.7, 6.8 Hz, H-1), 4.13 (1H, br d, *J* = 6.4 Hz, H-19), 4.04 (1H, dd, *J* = 12.2, 11.7 Hz, H-1), 3.03 (1H, dt, *J* = 6.8, 6.4 Hz, H-4), 2.49 (1H, ddd, *J* = 13.2, 9.3, 7.8 Hz, H-9), 2.33 (1H, dd, *J* = 12.2, 8.8 Hz, H-10), 2.20 (1H, m, H-6), 2.18 (1H, m, H-10), 2.13 (2H, m, H-13), 2.11 (1H, m, H-4a), 2.05 (1H, m, H-9), 2.03 (1H, m, H-11a), 1.99 (1H, m, H-6), 1.93 (1H, ddt, *J* = 14.2, 6.4, 6.8 Hz, H-12), 1.70 (3H, s, H-17), 1.65 (1H, m, H-5), 1.49 (1H, ddt, *J* = 14.2, 6.3, 6.8 Hz, H-12), 1.02 (1H, dddd, *J* = 13.7, 13.2, 10.3, 3.9 Hz, H-5); ^{13}C NMR data, see Table 1; HREIMS $(M)^+$ *m/z* obsd 304.2038; calcd for $C_{19}H_{28}O_3$, 304.2038 (Δ 0 mmu).

Acalycixeniolide L (8): amorphous solid; mp 137−140 °C; $[\alpha]^{25}_D$ 47.0° (*c* 0.12, MeOH); IR (KBr) ν_{max} 3400, 2930, 1745, 1640, 1450, 1390, 1145, 1025 cm^{-1}; ^{1}H NMR (CD_3OD) δ 5.68 (2H, m, H-14, H-15), 5.38 (1H, t, *J* = 7.8 Hz, H-8), 5.07 (1H, s, H-18), 5.00 (1H, s, H-18), 4.16 (1H, dd, *J* = 11.7, 6.8 Hz, H-1), 4.03 (1H, ddd, *J* = 11.7, 11.2, 1.0 Hz, H-1), 4.01 (2H, d, *J* = 5.0 Hz, H-16), 3.03 (1H, dt, *J* = 6.8, 6.3 Hz, H-4), 2.49 (1H, ddd, *J* = 12.7, 9.3, 8.8 Hz, H-9), 2.33 (1H, dd, *J* = 12.7, 8.8 Hz, H-10), 2.20 (1H, m, H-6), 2.18 (1H, m, H-10), 2.13 (2H, m, H-13), 2.11 (1H, m, H-4a), 2.06 (1H, m, H-9), 2.04 (1H, m, H-11a), 2.01 (1H, m, H-6), 1.92 (1H, ddt, *J* = 13.7, 6.8, 7.3 Hz, H-12), 1.70 (3H, s, H-17), 1.68 (1H, ddd, *J* = 13.2, 7.8, 4.4 Hz, H-5), 1.55 (1H, ddt, *J* = 13.7, 6.3, 6.8 Hz, H-12), 1.02 (1H, dddd, *J* = 13.2, 13.2, 9.2, 3.9 Hz, H-5); ^{13}C NMR data, see Table 1; HREIMS $(M)^+$ *m/z* obsd 304.2049; calcd for $C_{19}H_{28}O_3$, 304.2038 (Δ 1.0 mmu).

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(8) Due to the severe overlapping with each other, the coupling constant between H-14 and H-15 in the ^{1}H NMR spectra of **8** was not accurately measured.

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