# New Cytotoxic Butanolides from *Litsea acutivena*

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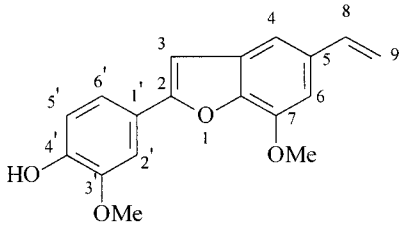
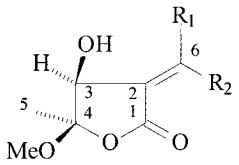
*Received May 7, 2001*

Six new compounds, including one nor-neolignan, dehydroxymethylailanthoidol (**1**), and five butanolides, litseakolide D (**2**), litseakolide E (**3**), litseakolide F (**4**), litseakolide G (**5**), and isolincomolide D (**6**), were isolated from the leaves of *Litsea acutivena*. Their structures were elucidated from spectral analyses. The butanolides (**2**−**6**) showed significant cytotoxic activity against P-388, A549, and HT-29 cell lines in vitro.

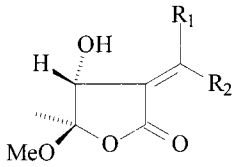
*Litsea acutivena* Hayata (Lauraceae) is an evergreen tree, distributed in southern China, Hainan Island, Indochina, and Taiwan.[1] Only one alkaloid, laurolitsine, has been reported from the wood of this species.[2] As an extension of our continuing studies on the cytotoxic constituents of Formosan plants, we have screened about 700 species for in vitro cytotoxicity, and *L. acutivena* was shown to be one of the active species. Investigation of the $CHCl_3$-soluble fraction of the leaves of this plant led to the isolation of six new compounds, namely, dehydroxymethylailanthoidol (**1**), litseakolide D (**2**), litseakolide E (**3**), litseakolide F (**4**), litseakolide G (**5**), and isolincomolide D (**6**). The isolation, structural elucidation, and cytotoxicity of these compounds are described herein.



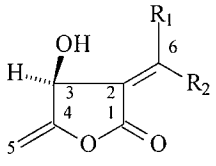
**1**



**2** $R_1$= $(CH_2)_8CH_3$, $R_2$= H
**3** $R_1$= H, $R_2$= $(CH_2)_8CH_3$



**4** $R_1$= $(CH_2)_8CH_3$, $R_2$= H
**5** $R_1$= H, $R_2$= $(CH_2)_8CH_3$



**6** $R_1$= H, $R_2$= $(CH_2)_{10}CH_3$

## Results and Discussion

Dehydroxymethylailanthoidol (**1**) was isolated as orange prisms, and the molecular formula, $C_{18}H_{16}O_4$, was determined by EIMS ($[M]^+$, *m*/*z* 296) and HR mass spectrometry. UV absorption bands at 313, 272, and 231 nm demonstrated that **1** was structurally related to a 2-phenyl-5-*trans*-ethenylbenzofuran-type compound.[3] The IR spectrum showed a hydroxyl absorption at 3365 $cm^{-1}$. The $^1H$ NMR spectrum for **1** was identical with that of the nor-neolignan, ailanthoidol,[3] except an ethenyl group [$\delta$ 6.79 (1H, dd, $J$ = 17.6, 10.8 Hz), 5.72 (1H, d, $J$ = 17.6, 0.8 Hz), 5.23 (1H, d, $J$ = 10.8, 0.8 Hz)] in **1** was in place of an (*E*)-3-hydroxy-1-propenyl group [$\delta$ 6.68 (1H, d, $J$ = 15.8 Hz), 4.35 (2H, d, $J$ = 5.7 Hz), 1.43 (1H, br s, OH)] in the C-5 position of the A-ring. Thus, the structure of **1** was elucidated as 2-(4-hydroxy-3-methoxyphenyl)-5-ethenyl-7-methoxybenzofuran, which was further confirmed by a negative Gibbs test and NOESY experiments (Figure 1). The isolation of **1** is the first report from a natural source, although it was mentioned as a pyrolytic product from humus.[4]

Litseakolide D (**2**) was isolated as a colorless oil. The molecular formula was determined to be $C_{16}H_{28}O_4$ by FABMS ($[M + H]^+$, *m*/*z* 285) and HRFAB mass spectrometry. The IR spectrum showed absorption bands for a hydroxyl group at 3444 $cm^{-1}$ and an $\alpha,\beta$-unsaturated-$\gamma$-lactone at 1763 and 1679 $cm^{-1}$. The $^1H$ NMR spectrum of **2** was similar to that of litsenolide $C_2$,[5,6] indicating the same $\beta$-hydroxy-$\gamma$-methyl-$\alpha,\beta$-unsaturated-$\gamma$-lactone structure and the same *E* geometry of the trisubstituted double bond [$\delta$ 6.95 (1H, td, $J$ = 8.0, 2.4 Hz, H-6)]. However, a methoxy group [$\delta$ 3.49 (3H, s)][7] in **2** replaced the H-4 [$\delta$ 4.50 (1H, qd, $J$ = 6.4, 2.0 Hz)] in litsenolide $C_2$, and the side chain was four methylene units shorter than that of litsenolide $C_2$. The absolute stereochemistry at C-3 was determined

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10.1021/np0102298 CCC: $20.00 
Published on Web 11/08/2001

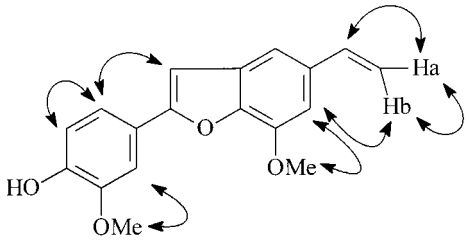
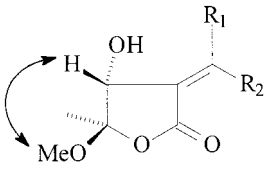



**Figure 1.** NOESY correlations of compound **1**.




**4** $R_1$= $(CH_2)_8CH_3$, $R_2$= H
**5** $R_1$= H, $R_2$= $(CH_2)_8CH_3$

**Figure 2.** NOESY correlations of compounds **4** and **5**.

to be 3*S* based on the correlation between the $[\alpha]_D$ value [−73.3° (*c* 0.13, $CHCl_3$)] and the known configuration at C-3 for 2-alkylidene-3-hydroxy-4-methylbutanolide derivatives.[5,6,8−10] The stereochemistry of C-4 was determined to be 4*R* from the NOESY spectrum (Figure 2), which showed no correlation between the H-3 and methoxyl signals, indicating that H-3 and methoxyl group are *trans*. From the above evidence, the structure of litseakolide D was represented by the formula **2**, which was further confirmed by $^{13}C$ NMR, DEPT, and HMQC experiments.

Litseakolide E (**3**) was isolated as a colorless oil. The FABMS afforded the positive ion $[M + H]^+$ at *m*/*z* 285, implying a molecular formula of $C_{16}H_{28}O_4$. The IR spectrum showed absorption bands for a hydroxyl group at 3442 $cm^{-1}$ and an α,*β*-unsaturated-*γ*-lactone at 1766 and 1679 $cm^{-1}$. From the spectral evidence, compound **3** was similar to **2** and has the same *β*-hydroxy-*γ*-methyl-α,*β*-unsaturated-*γ*-lactone structure. The major difference was the *Z*-form geometry of the trisubstituted double bond [*δ* 6.45 (1H, td, *J* = 8.0, 2.4 Hz, H-6)]. The $[\alpha]_D$ value [−83.2° (*c* 0.20, $CHCl_3$)] once again indicated the stereochemistry of C-3 as 3*S*, and the NOESY spectrum, which also showed no correlation between H-3 and methoxyl signals, suggested the *R* configuration at C-4. From the above data, the structure of litseakolide E was represented by the formula **3**, which was further confirmed by $^{13}C$ NMR, DEPT, COSY, and HETCOR experiments.

Litseakolide F (**4**) was isolated as a colorless oil. The molecular formula was determined to be $C_{16}H_{28}O_4$ by FABMS ($[M + H]^+$, *m*/*z* 285) and HRFAB mass spectrometry. The IR spectrum showed absorption bands for a hydroxyl group at 3431 $cm^{-1}$ and an α,*β*-unsaturated-*γ*-lactone at 1746 and 1679 $cm^{-1}$. The $^1H$ NMR spectrum data were similar to that of **2** and showed the same *β*-hydroxy-*γ*-methyl-α,*β*-unsaturated-*γ*-lactone structure and the same *E* geometry of the trisubstituted double bond [*δ* 6.95 (1H, td, *J* = 8.0, 1.2 Hz, H-6)]. The major difference was the positive $[\alpha]_D$ value [+54.3° (*c* 0.49, $CHCl_3$)], so the stereochemistry of C-3 was determined to be 3*R*.[7] The NOESY spectrum showed correlations between the H-3 and methoxyl signals, supporting the 4*R* stereochemistry (Figure 2). Despite the long chain, the chemical shifts of signals on **4** are the same as those on (2*E*,3*R*,4*R*)-2-(11-dodecenylidene)-3-hydroxy-4-methoxy-4-methylbutanolide.[8] From the above observations, the structure of litseakolide F was represented by the formula **4** and was further confirmed by $^{13}C$ NMR, DEPT, COSY, and HETCOR experiments.

Litseakolide G (**5**) was isolated as a colorless oil, with molecular formula $C_{16}H_{28}O_4$, as established by FABMS ($[M + H]^+$, *m*/*z* 285) and HRFAB mass spectrometry. The IR spectrum showed absorption bands for a hydroxyl group at 3439 $cm^{-1}$ and an α,*β*-unsaturated-*γ*-lactone at 1753 and 1672 $cm^{-1}$. The $^1H$ NMR spectrum data were similar to that of **3**; thus **5** has the same *β*-hydroxy-*γ*-methyl-α,*β*-unsaturated-*γ*-lactone structure and the same *Z* geometry of the trisubstituted double bond [*δ* 6.56 (1H, td, *J* = 8.0, 1.2 Hz, H-6)]. Again, the major difference was in the positive $[\alpha]_D$ value [+77.4° (*c* 0.09, $CHCl_3$)], suggesting the 3*R* stereochemistry of C-3.[8] The stereochemistry of C-4 was determined to be 4*R* from the NOESY spectrum (Figure 2), which showed the expected correlations between the H-3 and methoxyl signals. Thus, the structure of litseakolide G was represented by formula **5** and was further confirmed by $^{13}C$ NMR, DEPT, COSY, and HETCOR experiments.

Isolincomolide D (**6**) was isolated as a colorless oil, with molecular formula $C_{17}H_{28}O_3$, determined by FABMS ($[M + 1]^+$, *m*/*z* 281) and HRFAB mass spectrometry. The IR spectrum showed absorption bands for a hydroxyl group at 3449 $cm^{-1}$ and an α,*β*-unsaturated-*γ*-lactone at 1781 and 1679 $cm^{-1}$. The $[\alpha]_D$ value [−49.5° (*c* 0.20, $CHCl_3$)] indicated the 3*S* configuration.[8] The $^1H$ NMR spectrum data were similar to that of lancifolide,[11] with the same *β*-hydroxy-*γ*-methylene-α,*β*-unsaturated-*γ*-lactone structure and *Z* trisubstituted double bond [*δ* 6.69 (1H, td, *J* = 8.0, 2.0 Hz, H-6)]. Thus, the structure of isolincomolide D was represented by formula **6** and was further confirmed by $^{13}C$ NMR, DEPT, COSY, and HETCOR experiments.

The cytotoxic activity of compounds **1**−**6** were tested in vitro against P-388, A549, and HT-29 cell lines (Table 3). Compounds **2**−**6** showed good cytotoxicity against all three cell lines. With a fixed configuration of 3*S*,4*R*, the *E*-configured isomer **2** showed stronger cytotoxicity than the *Z*-form butanolide **3**, and with the 3*R*,4*R* configuration, the *Z*-isomer **5** showed stronger cytotoxicity than the *E* butanolide **4**. In comparison of butanolides **2** and **4**, which both contain an *E*-configured double bond, **2** was more cytotoxic against P-388 and HT-29 cell lines, but less cytotoxic against the A549 cell line. With the *Z*-form-configured isomers **3** and **5**, compound **5** was more cytotoxic against all three cell lines. Compared with lincomolide D (*E*-form),[12] **6** was less cytotoxic against the P-388 cell line, but more cytotoxic against the HT-29 and A549 cell lines. The cytotoxicity of these butanolides is likely attributed to the presence of the α,*β*-unsaturated lactone, which can undergo Michael addition with biological nucleophiles. Naturally occurring sesquiterpene lactones, such as helenalin, also possess a O=C−C=C system, which has been linked to their cytotoxic activity.[13−15] No cytotoxic selectivity was observed for compounds **2**−**6**, as can be observed in Table 3.

## Experimental Section

**General Experimental Procedures**. Melting points were determined with a YANACO micro-melting point apparatus and are uncorrected. Optical rotations were measured using a JASCO DIP-370 polarimeter in $CHCl_3$. IR spectra were taken on a Hitachi 260-30 (KBr and neat) spectrophotometer. UV spectra were obtained on a JASCO UV-240 spectrophotometer. MS spectra were recorded on a VG Biotech Quattro 5022 spectrometer. HRMS were recorded on a JEOL JMX-HX 110 mass spectrometer. $^1H$ NMR and $^{13}C$ NMR spectra were measured on either a Varian Unity Plus 400 or JEOL GSX-600 spectrometer and are given in ppm (*δ*) downfield from

**Table 1.** $^1$H NMR Data for Butanolides **2**−**5** (400 MHz, $CDCl_3$)

| H | **2** | **3** | **4** | **5** |
|---|---|---|---|---|
| 3 | 4.63 (1H, br d, $J$ = 8.8 Hz) | 4.43 (1H, br d, $J$ = 8.8 Hz) | 4.52 (1H, br s) | 4.40 (1H, br s) |
| 5 | 1.62 (3H, s) | 1.62 (3H, s) | 1.61 (3H, s) | 1.55 (3H, s) |
| 6 | 6.95 (1H, td, $J$ = 8.0, 2.4 Hz) | 6.45 (1H, td, $J$ = 8.0, 2.4 Hz) | 6.95 (1H, td, $J$ = 8.0, 1.2 Hz) | 6.56 (1H, td, $J$ = 8.0, 1.2 Hz) |
| 7 | 2.46 (2H, m) | 2.70 (2H, m) | 2.38 (2H, m) | 2.75 (2H, m) |
| 8 | 1.48 (2H, m) | 1.46 (2H, m) | 1.52 (2H, m) | 1.47 (2H, m) |
| 9−14 | 1.26 (12H, br s) | 1.26 (12H, br s) | 1.27 (12H, br s) | 1.26 (12H, br s) |
| 15 | 0.88 (3H, t, $J$ = 6.8 Hz) | 0.88 (3H, t, $J$ = 6.8 Hz) | 0.88 (3H, t, $J$ = 6.8 Hz) | 0.88 (3H, t, $J$ = 6.8 Hz) |
| $OCH_3$ | 3.49 (3H, s) | 3.44 (3H, s) | 3.37 (3H, s) | 3.40 (3H, s) |
| OH | 2.84 (1H, br d, $J$ = 8.8 Hz) | 2.53 (1H, br d, $J$ = 8.8 Hz) | 2.61 (1H, br s) | 2.09 (1H, br s) |

**Table 2.** $^{13}$C NMR Data for Butanolides **2**−**5** (100 MHz, $CDCl_3$)

| C | **2** | **3** | **4** | **5** |
|---|---|---|---|---|
| 1 | 168.1 | 166.9 | 169.3 | 167.3 |
| 2 | 128.4 | 128.1 | 130.0 | 129.0 |
| 3 | 74.1 | 75.9 | 72.4 | 75.8 |
| 4 | 103.9 | 103.9 | 109.7 | 108.8 |
| 5 | 19.9 | 19.1 | 16.0 | 16.3 |
| 6 | 147.9 | 147.3 | 148.4 | 150.3 |
| 7 | 29.47 | 27.74 | 29.78 | 28.04 |
| 8 | 28.52 | 28.90 | 28.34 | 28.77 |
| 9 | 28.87 | 29.24 | 29.22 | 29.22 |
| 10 | 29.27 | 29.30 | 29.31 | 29.25 |
| 11 | 29.33 | 29.42 | 29.42 | 29.37 |
| 12 | 29.37 | 29.53 | | 29.47 |
| 13 | 31.9 | 31.9 | 31.8 | 31.8 |
| 14 | 22.7 | 22.7 | 22.6 | 22.6 |
| 15 | 14.1 | 14.1 | 14.0 | 14.1 |
| $OCH_3$ | 50.7 | 50.3 | 50.2 | 50.4 |

(**2**: $C_9$−$C_{12}$; **3**: $C_9$−$C_{12}$; **4**: $C_9$−$C_{12}$; **5**: $C_9$−$C_{12}$)

**Table 3.** Cytotoxicity of Compounds **1**−**6**

| compound | $ED_{50}$ ($\mu$g mL$^{-1}$) P-388 | A549 | HT-29 |
|---|---|---|---|
| dehydroxymethylailanthoidol (**1**) | >50 | >50 | >50 |
| litseakolide D (**2**) | 1.73 | 2.85 | 2.00 |
| litseakolide E (**3**) | 2.94 | 4.89 | 3.69 |
| litseakolide F (**4**) | 2.04 | 2.01 | 4.39 |
| litseakolide G (**5**) | 0.97 | 1.94 | 2.73 |
| isolincomolide D (**6**) | 2.97 | 2.90 | 2.11 |
| mithramycin[a] | 0.06 | 0.07 | 0.08 |

[a] Positive control

internal TMS. Silica gel 60 (Merck 70-230 mesh, 230−400 mesh, ASTM) was used for CC and silica gel 60 $F_{254}$ (Merck) for TLC.

**Plant Material.** Leaves of *L. acutivena* Hayata were collected from Li-Long mountain, Pintung county, Taiwan, in September 1999. A voucher specimen (no. Chen 6096) is deposited in the Herbarium of the School of Pharmacy, Kaohsiung Medical University, Taiwan, Republic of China.

**Extraction and Isolation**. Dried leaves (8.7 kg) were extracted with MeOH and concentrated in vacuo to leave a brownish fluid. The MeOH extract was partitioned between $CHCl_3$ and $H_2O$ (1:1). The $H_2O$-soluble fraction was further partitioned between $H_2O$ and *n*-BuOH (1:1) to afford a $H_2O$ fraction (fraction D, 390 g) and an *n*-BuOH fraction (fraction C, 250 g). The $CHCl_3$-soluble fraction was partitioned between 90% aqueous MeOH and *n*-hexane (1:1), giving an *n*-hexane fraction (fraction B, 150 g) and a $CHCl_3$ fraction (fraction A, 180 g). A part of fraction A (100 g) was chromatographed over Si gel, eluting with a $CHCl_3$−MeOH gradient, to obtain 15 fractions (A1−A15). Fraction A5 (4.34 g, $CHCl_3$−MeOH, 100:1) was resubjected to Si gel chromatography, eluting with *n*-hexanes−EtOAc (50:1) enriched gradually with EtOAc to obtain 24 fractions (A5-1−A5-24). Fraction A5-16 (59.5 mg, *n*-hexanes−EtOAc, 10:1) was resubjected to Si gel CC and purified by preparative TLC ($CHCl_3$−EtOAc, 15:1) to yield **1** (1.1 mg), **2** (2.2 mg), and **3** (3.1 mg). Fraction A7 (10.8 g, $CHCl_3$−MeOH, 100:1) was resubjected to Si gel, eluting with *n*-hexanes−EtOAc (50:1) enriched gradually with EtOAc to obtain 28 fractions (A7-1−A7-28). Fraction A7-8 (1.38 g, *n*-hexanes−EtOAc, 10:1) was resubjected to Si gel CC and purified by preparative TLC ($CHCl_3$−EtOAc, 50:1) to yield **6** (4.1 mg). Fraction A7-13 (0.96 g, *n*-hexanes−EtOAc, 10:1) was resubjected to Si gel CC and purified by preparative TLC ($CHCl_3$−EtOAc, 50:1) to yield **4** (24.4 mg) and **5** (8.2 mg).

**Method for Cytotoxicity Assay.** P-388 cells were kindly provided by Prof. J. M. Pezzuto, University of Illinois at Chicago; A549 (human lung adenocarcinoma) and HT-29 (human colon carcinoma) were purchased from American Type Culture Collection.

P-388 cells were cultured in Fisher's medium supplemented with 10% heat-inactivated (56 °C for 30 min) fetal calf serum (FCS). A549 cells were cultured in Eagle Minimum Essential medium (EMEM) containing Earle's salts and supplemented with 0.1 mM nonessential amino acids and 10% heat-inactivated FCS. HT-29 cells were maintained in Rosewell Park Memorial Institute (RPMI) 1640 medium containing 10% heat-inactivated FCS. All cell lines were maintained in an incubator at 37 °C in humidified air containing 5% $CO_2$.

The cytotoxic activities of compounds against P-388, A549, and HT-29 were assayed by a modification of the MTT [3-(4,5-dimethylthiazole-2-yl)-2,5-diphenyltetrazolium bromide] colorimetric method.[16] For P-388 cells, 200 $\mu$L cultures were established at 1500 cells/well in 96-well tissue culture plates (Falcon). Compounds were dispensed to established cultures

at eight concentrations in triplicate. After 3 days of incubation, P-388 cells were enumerated with MTT.

To measure the cytotoxic activities of purified compounds against A549 and HT-29 cells, each cell line was initiated at 1000 cells/well in 96-well microtiter plates. Eight concentrations (triplicate) of test compounds encompassing a 128-fold range were added to each cell line. A549 and HT-29 cells were enumerated using MTT after exposure to test compounds for 6 days, respectively. Fifty microliters of 1 mg/mL MTT was added to each well, and plates were incubated at 37 °C for a further 5 h. Formazan crystals were redissolved in DMSO (E. Merck) for 10 min with shaking, and the plate was read immediately on a microtiter plate reader (Dynatech) at a wavelength of 540 nm. The $ED_{50}$ was defined as the concentration of the test compound resulting in a 50% reduction of absorbance compared to untreated cells in the MTT assay.

**Dehydroxymethylailanthoidol (1):** orange prisms (MeOH); mp 186−187 °C; UV (EtOH) $\lambda_{max}$ (log $\epsilon$) 313 (3.67), 272 (3.64), 231 (3.68) nm; IR (KBr) $\nu_{max}$ 3365 (OH) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 4.00 (3H, s, OMe-3′), 4.07 (3H, s, OMe-7), 5.23 (1H, d, $J$ = 10.8, 0.8 Hz, H-9a), 5.72 (1H, d, $J$ = 17.6, 0.8 Hz, H-9b), 5.76 (1H, br s, OH-4′), 6.79 (1H, dd, $J$ = 17.6, 10.8 Hz, H-8), 6.85 (1H, s, H-3), 6.89 (1H, d, $J$ = 1.6 Hz, H-6), 6.98 (1H, d, $J$ = 8.0 Hz, H-5′), 7.17 (1H, d, $J$ = 1.6 Hz, H-4), 7.37 (1H, d, $J$ = 2.0 Hz, H-2′), 7.40 (1H, dd, $J$ = 8.0, 2.0 Hz, H-6′); EIMS $m/z$ 296 $[M]^+$ (100); HREIMS $m/z$ 296.1046 (calcd for $C_{18}H_{16}O_4$, 296.1049).

**Litseakolide D (2):** colorless oil; $[\alpha]\ ^{25}_D$ −73.3° ($c$ 0.13, $CHCl_3$); UV (EtOH) $\lambda_{max}$ (log $\epsilon$) 221(3.08) nm; IR (neat) $\nu_{max}$ 3444 (OH), 1763, 1679 (α,$\beta$-unsaturated-$\gamma$-lactone) $cm^{-1}$; $^1H$ NMR, Table 1; $^{13}C$ NMR, Table 2; FABMS $m/z$ 285 $[M + H]^+$ (72); HRFABMS $m/z$ 285.2064 (calcd for $C_{16}H_{29}O_4$, 285.2066).

**Litseakolide E (3):** colorless oil; $[\alpha]^{25}_D$ −83.2° ($c$ 0.20, $CHCl_3$); UV (EtOH) $\lambda_{max}$ (log $\epsilon$) 221(3.24) nm; IR (neat) $\nu_{max}$ 3442 (OH), 1766, 1679 (α,$\beta$-unsaturated-$\gamma$-lactone) $cm^{-1}$; $^1H$ NMR, Table 1; $^{13}C$ NMR, Table 2; FABMS $m/z$ 285 $[M + H]^+$ (24).

**Litseakolide F (4):** colorless oil; $[\alpha]^{25}_D$ +54.3° ($c$ 0.49, $CHCl_3$); UV (EtOH) $\lambda_{max}$ (log $\epsilon$) 220(3.44) nm; IR (neat) $\nu_{max}$ 3431 (OH), 1746, 1679 (α,$\beta$-unsaturated-$\gamma$-lactone) $cm^{-1}$; $^1H$ NMR, Table 1; $^{13}C$ NMR, Table 2; FABMS $m/z$ 285 $[M + H]^+$ (100); HRFABMS $m/z$ 285.2061 (calcd for $C_{16}H_{29}O_4$, 285.2066).

**Litseakolide G (5):** colorless oil; $[\alpha]^{25}_D$ +77.4° ($c$ 0.09, $CHCl_3$); UV (EtOH) $\lambda_{max}$ (log $\epsilon$) 221(3.37) nm; IR (neat) $\nu_{max}$ 3439 (OH), 1753, 1672 (α,$\beta$-unsaturated-$\gamma$-lactone) $cm^{-1}$; $^1H$ NMR, Table 1; $^{13}C$ NMR, Table 2; FABMS $m/z$ 285 $[M + H]^+$ (91); HRFABMS $m/z$ 285.2057 (calcd for $C_{16}H_{29}O_4$, 285.2065).

**Isolicomolide D (6):** colorless oil; $[\alpha]^{25}_D$ −49.5° ($c$ 0.20, $CHCl_3$); UV (EtOH) $\lambda_{max}$ (log $\epsilon$) 226(3.64) nm; IR (neat) $\nu_{max}$ 3449 (OH), 1781, 1679 (α,$\beta$-unsaturated-$\gamma$-lactone) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 0.88 (3H, t, $J$ = 6.4 Hz, H-17), 1.26 (16H, br s, H-9−16), 1.49 (2H, m, H-8), 2.05 (1H, br s, OH-3), 2.77 (2H, m, H-7), 4.67 (1H, dd, $J$ = 2.8, 1.6 Hz, H-5a), 4.89 (1H, dd, $J$ = 2.8, 2.0 Hz, H-5b), 5.11 (1H, br d, $J$ = 1.6 Hz, H-3), 6.69 (1H, td, $J$ = 8.0, 2.0 Hz, H-6); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 14.1 (C-17), 22.6 (C-16), 28.3 (C-7), 28.7 (C-8), 28.95, 29.24, 29.34, 29.43, 29.71 (C-9−14), 31.8 (C-15), 66.8 (C-3), 90.2 (C-5), 126.8 (C-2), 151.3 (C-6), 157.5 (C-4), 165.2 (C-1); FABMS $m/z$ 280 $[M + H]^+$ (10); HRFABMS $m/z$ 281.2100 (calcd for $C_{17}H_{29}O_3$, 281.2116).

**Acknowledgment.** This work was kindly supported by the National Science Council of the Republic of China (NSC89-2314-B-037-045). We are grateful to Prof. Tsutomu Ishikawa (Chiba University, Japan) for assistance with measurement of FABHRMS and COSY spectra.

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NP0102298