ent-Kaurane Diterpenoids from *Annona glabra*

Chung-Yi Chen, Fang-Rong Chang, Chun-Ping Cho, and Yang-Chang Wu*

Graduate Institute of Natural Products, Kaohsiung Medical University, Kaohsiung 807, Taiwan, Republic of China

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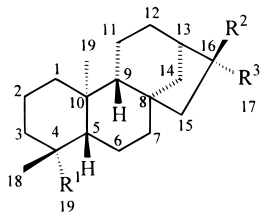
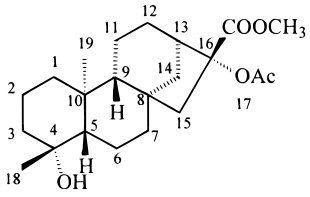
Three new kaurane diterpenoids, annoglabasin C (16α-acetoxy-*ent*-kauran-19-oic acid-17-methyl ester) (**1**), annoglabasin D (16α-acetoxy-*ent*-kauran-19-al-17-methyl ester) (**2**), and annoglabasin E (16α-hydro-19-ol-*ent*-kauran-17-oic acid) (**3**), and a new norkaurane diterpenoid, annoglabasin F (16α-acetoxy-19-nor-*ent*-kauran-4α-ol-17-methyl ester) (**4**), along with 13 known kaurane derivatives were isolated from the stems of *Annona glabra*. 16α-Methoxy-*ent*-kauran-19-oic acid (**5**) and 16α-hydro-*ent*-kauran-17,19-dimethyl ester (**6**) were obtained for the first time as natural products. The structures of compounds **1**−**6** were characterized by spectral analysis.

Annona glabra L. (Annonaceae), commonly known as "pond apple", is a tropical tree distributed mainly in the Americas and in southeast Asia. It has been used as an insecticide and a parasiticide.[1,2] Recently, we have reported two new kaurane diterpenoids, annoglabasins A and B, together with 11 known kaurane diterpenoids from the fresh fruits of *A. glabra*.[3] Among these, methyl-16α-hydro-19-al-*ent*-kauran-17-oate exhibited mild activity against HIV replication in H9 lymphocyte cells, and 16α,17-dihydroxy-*ent*-kauran-19-oic acid showed significant inhibition of HIV-reverse transcriptase.[3] In continuation of a program toward the studies of chemotaxonomy and biologically active metabolites from the Annonaceous plants, a MeOH extract of the stems of *A. glabra* has afforded three new kaurane diterpenoids, annoglabasins C (16α-acetoxy-*ent*-kauran-19-oic acid-17-methyl ester) (**1**), D (16α-acetoxy-*ent*-kauran-19-al-17-methyl ester) (**2**), and E (16α-hydro-19-ol-*ent*-kauran-17-oic acid) (**3**), a new norkaurane diterpenoid, annoglabasin F (16α-acetoxy-19-nor-*ent*-kauran-4α-ol-17-methyl ester) (**4**); and 13 known compounds, 16α-methoxy-*ent*-kauran-19-oic acid (**5**),[3,4] 16α-hydro-*ent*-kauran-17,19-dimethyl ester (**6**),[5] 16*β*,17-dihydroxy-*ent*-kauran-19-oic acid,[6,7] 16*β*,17-diacetoxy-*ent*-kauran-19-oic acid,[8] 16α-hydro-*ent*-kauran-17,19-dioic acid,[9] *ent*-kaur-16-en-19-oic acid,[10] 16α-hydro-19-al-*ent*-kauran-17-oic acid,[11] 16α-hydro-19-al-*ent*-kauran-17-methyl ester,[3] 16α-hydroxy-*ent*-kauran-19-oic acid,[12] 16α-hydro-*ent*-kauran-17-oic acid,[13] *ent*-kaur-15-en-17-ol-19-oic acid,[14] *ent*-kaur-15-en-17,19-diol,[3,15,16] and 19-nor-*ent*-kauran-4α-ol-17-oic acid.[9,11] In addition to the four new compounds, **5** and **6** were isolated for the first time as natural products although they have been synthesized previously.[5,17]



	R^1	R^2	R^3
1	COOH	$COOCH_3$	OAc
2	CHO	$COOCH_3$	OAc
3	CH_2OH	COOH	H
5	COOH	CH_3	OCH_3
6	$COOCH_3$	$COOCH_3$	H



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Annoglabasin C (**1**) was obtained as a white powder, $[\alpha]^{25}_D$ -141.0° (*c* 0.18, $CHCl_3$), which was positive to the Liebermann−Burchard reaction. Its IR spectrum showed absorption bands at 1745 and 1690 cm^{-1} due to ester carbonyl and carboxylic acid functions, respectively. The HRFABMS of compound **1** showed a pseudomolecular ion $[M + 1]^+$ at *m/z* 407.2451, corresponding to the molecular formula, $C_{23}H_{34}O_6$. The ^{13}C NMR spectrum and a DEPT experiment indicated that **1** has a total of 23 carbons. Except for the acetoxyl and methoxyl groups, the main skeleton of **1** consists of 20 carbons, which is consistent with an *ent*-kaurane diterpenoid.[3,4] The ^1H NMR spectrum of **1** ($CDCl_3$) exhibited signals for two tertiary methyl groups at *δ* 1.23 and 0.92, which are typical for equatorial C-18 and axial C-20 methyl groups of an *ent*-kaurane diterpenoid with a C-19 axial carboxylic acid group.[3,4] The other major features of the ^1H NMR spectrum of **1** were a methine signal at *δ* 2.37, an acetoxyl signal at *δ* 2.04, and a carbomethoxyl signal at *δ* 3.71. The ^{13}C NMR spectrum of **1** and DEPT experiments showed 23 resonance lines consisting of four methyls at *δ* 28.8 (C-18), 15.4 (C-20), 21.1 (acetoxyl methyl group), and 52.2 (methyl carbon of carbomethoxyl); nine methylenes between *δ* 17.0 and 51.1; three methines at *δ* 56.5 (C-5), 55.2 (C-9), and 46.1 (C-13); and seven quaternary carbons at *δ* 39.6 (C-10), 44.8 (C-8), 43.7 (C-4), 89.1 (C-16, acetoxyl-bearing carbon), 170.5 (C-17, ester carbonyl carbon), 171.0 (acetoxyl carbonyl carbon), and 184.0 (C-19, carboxylic acid carbon). Comparison of these ^{13}C NMR chemical shifts with those of related kauranoid diterpenes, suggested that **1** possesses an *ent*-

* To whom correspondence should be addressed. Tel.: +886-7-3121101, ext. 2197. Fax: +886-7-3114773. E-mail: yachwu@cc.kmu.edu.tw.

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kaurane-type skeleton with a carboxylic acid located at C-19.[18,19] The missing signals for H-16 and the appearance of the H-13 signal at δ 2.37 suggested the presence of an acetyl group at C-16 and a carbomethoxyl group at C-17 as in annoglabasin A.[3] The relative configuration of the acetoxyl group of **1** was determined using a NOESY experiment, in which a correlation between H-13 and the acetoxyl group was evident. The stereochemistry of the acetoxyl group was assigned in the α position in **1**. The structure of **1** was further confirmed by a peak appearing at *m/z* 347, indicating the facile loss of $COOCH_3$ or OAc, and by other fragments, which were found at *m/z* 375 [M − OCH_3], 347 [375 − CO], 314, 300, 121, 109, and 91 in the EIMS. Thus, the structure of **1** was determined to be 16α-acetoxy-*ent*-kauran-19-oic acid-17-methyl ester, which we have named annoglabasin C.

Annoglabasin D (**2**) was obtained as a white powder. Its IR spectrum showed absorption bands at 1747 and 1715 cm^{-1} due to ester carbonyl and aldehyde functions, respectively. The HRFABMS of compound **2** showed a pseudomolecular ion $[M + 1]^+$ at *m/z* 391.2477, corresponding to the molecular formula, $C_{23}H_{34}O_5$. The ^1H and ^{13}C NMR spectra of **2** were similar to those of **1** except for the presence of an aldehyde moiety (δ 9.69 and 205.7). Comparison of these ^{13}C NMR chemical shifts with those of related kauranoid diterpenes suggested that **2** possessed the same *ent*-kaurane-type skeleton with an aldehyde located at C-19.[3,9,11] The relative configuration of the acetoxyl group of **2** again followed from a NOESY experiment, which showed the correlation between H-13 with the acetoxyl group. Thus, the acetoxyl group was assigned with α stereochemistry. In the EIMS, fragments appeared at *m/z* 331 [M − $COOCH_3$ or OAc], 300 [331 − OCH_3], 272 [300 − CO], 233, 123, 109, and 91, which are the same as those of annoglabasin A.[3] Thus, the structure of **2** was determined to be 16α-acetoxy-*ent*-kauran-19-al-17-methyl ester, which we have named annoglabasin D.

Annoglabasin E (**3**) was obtained as a white powder. The major IR absorption band was characteristic of carbonyl at ν_{max} 1725 cm^{-1}. The HRFABMS of compound **3** showed a pseudomolecular ion $[M + 1]^+$ at *m/z* 321.2415, corresponding to the molecular formula $C_{20}H_{32}O_3$. The ^1H NMR spectrum of **3** displayed methyl singlets at δ 0.99 and 1.20, a pair of doublets at δ 4.04 and 3.67, and two methine protons at δ 2.73 and 3.17, indicating that **3** was probably an *ent*-kaurane diterpene possessing a carboxylic acid at C-17 and a hydroxy group at C-19.[3,9,11,15,16] The carbons of the *ent*-kaurane diterpene were assigned, from ^{13}C NMR and DEPT experiments, as two methyls at δ 18.4 (C-20) and 28.0 (C-18); 10 methylenes [including a hydroxy-bearing methylene at δ 64.1 (C-19)]; four methines at δ 40.1 (C-13), 46.9 (C-16), 57.0 (C-9), and 57.6 (C-5); and four quaternary carbons at δ 39.1 (C-4), 39.3 (C-10), 44.6 (C-8), and a carboxylic acid carbon at δ 176.9 (C-17). The stereochemical relationship of H-16 was α in **3** as determined by the NOESY spectrum, which showed a correlation between H-13 and H-16. The structure of **3** was further confirmed by a base peak appearing at *m/z* 289, indicating the facile loss of CH_2OH, and other fragments were found at *m/z* 271 [289 − H_2O], 243 [271 − CO], 192, 123, 109, and 107 in the EIMS. Thus, the evidence described above indicated that **3** is 16α-hydro-19-ol-*ent*-kauran-17-oic acid, a new *ent*-kaurane diterpene. To clarify the nomenclature of 16-hydro kaurane diterpenes (e.g., compound **3**), we have defined the orientation of H-16 by using the terminology "16α-hydro" or "16β-hydro" to indicate the stereochemistry.[2,3]

Annoglabasin F (**4**) was obtained as a white powder. Its IR spectrum showed absorption bands both at 3400 and 1745 and 1690 cm^{-1} due to hydroxyl group and ester carbonyl functions, respectively. The HRFABMS of compound **4** showed a pseudomolecular ion $[M + 1]^+$ at *m/z* 379.2489, corresponding to the molecular formula, $C_{22}H_{34}O_5$. The ^{13}C NMR spectrum and a DEPT experiment indicated that **4** had a total of 22 carbons, with the skeleton consisting of 19 carbons, consistent with a nor-*ent*-kaurane diterpenoid.[9,11] The ^{13}C NMR spectrum of **4** and DEPT experiments showed 22 resonance lines consisting of four methyls at δ 22.6 (C-18), 16.8 (C-19), 21.0 (acetoxyl methyl group), and 52.1 (methyl carbon of carbomethoxyl); nine methylenes between δ 16.9 and 51.2; three methines at δ 57.2 (C-5), 55.8 (C-9), and 46.1 (C-13); and six quaternary carbons at δ 39.7 (C-10), 44.6 (C-8), 72.2 (C-4), 89.1 (C-16, acetoxyl-bearing carbon), 170.8 (acetoxyl carbonyl carbon), and 171.3 (C-17, ester carbonyl carbon). The ^1H NMR spectrum of **4** ($CDCl_3$) showed signals for two tertiary methyl groups at δ 1.10 and 0.95, typical of equatorial C-18 and axial C-19 methyl groups of a 4-hydroxynor-*ent*-kaurane diterpenoid.[3,4,9,11] The other major features of the ^1H NMR spectrum of **4** were a methine signal at δ 2.39, an acetoxyl signal at δ 2.03, and a carbomethoxyl signal at δ 3.71. Comparison of these ^{13}C NMR chemical shifts with those of the related norkauranoid diterpene 19-nor-*ent*-kauran-4α-ol-17-oic acid suggested that **4** possesses the same nor-*ent*-kaurane-type skeleton.[9,11] The typical C-4 at δ 72.2 of norkauranoid diterpene was much different from the kauranoid diterpene in the ^{13}C NMR spectrum, owing to a hydroxy group attached to C-4. The missing signals for H-16 and the typical proton shift of H-13 suggested the presence of an acetyl group at C-16 and a carbomethoxyl at C-17. The relative configuration of the acetoxyl group in **4** was determined using a NOESY experiment, in which a correlation between H-13 with acetoxyl group was evident. The acetoxyl group was determined as α in **4** proven by the NOESY spectrum. The structure of **4** was further confirmed by peaks appearing at *m/z* 361 [M − OH], 302 [361 − $COOCH_3$ or OAc], 271 [301 − OCH_3], 243 [271 − CO], 105, and 91 in the EIMS. Thus, the structure of **4** was determined to be 16α-acetoxy-19-nor-*ent*-kauran-4α-ol-17-methyl ester, which we have named annoglabasin F.

After the structure elucidation of 16α-methoxy-*ent*-kauran-19-oic acid (**5**) and 16α-hydro-*ent*-kauran-17,19-dimethyl ester (**6**) by spectral means, it was determined that these two compounds had been prepared synthetically previously.[5,17]

Experimental Section

General Experimental Procedures. Melting points were determined using a Yanagimoto micro-melting point apparatus and are uncorrected. Optical rotations were measured with a JASCO DIP-370 digital polarimeter. The IR spectra were measured on a Hitachi 260−30 spectrophotometer. ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded with Varian NMR spectrometers, using TMS as internal standard. LRFABMS and LREIMS were obtained with a JEOL JMS−SX/SX 102A mass spectrometer or a Quattro GC/MS spectrometer having a direct inlet system. HRFABMS were measured on a JEOL JMS−HX 110 mass spectrometer. Si gel 60 (Macherey-Nagel, 230−400 mesh) was used for column chromatography, precoated Si gel plates (Macherey-Nagel, SIL G-25 UV_{254}, 0.25 mm) were used for analytical TLC, and precoated Si gel plates (Macherey-Nagel, SIL G/UV_{254}, 0.25 mm) were used for preparative TLC. The spots were detected by spraying with 50% H_2SO_4 and then heating on a hot plate.

Plant Material. The stems of *A. glabra* were collected from Chia-Yi City, Taiwan, in August 1996. A voucher specimen is

Table 1. ^{13}C NMR Chemical Shifts Values for Diterpenes **1**−**4** (100 MHz, δ in ppm)

carbon	**1** (mult.)	**2** (mult.)	**3** (mult.)	**4** (mult.)
1	41.6 (t)	41.5 (t)	40.8 (t)	42.8 (t)
2	18.9 (t)	18.2 (t)	18.4 (t)	19.0 (t)
3	37.7 (t)	34.2 (t)	36.1 (t)	37.7 (t)
4	43.7 (s)	48.3 (s)	39.1 (s)	72.2 (s)
5	56.5 (d)	56.2 (d)	57.6 (d)	57.2 (d)
6	21.9 (t)	19.9 (t)	21.0 (t)	19.4 (t)
7	37.8 (t)	37.9 (t)	42.4 (t)	39.1 (t)
8	44.8 (s)	44.6 (s)	44.6 (s)	44.6 (s)
9	55.2 (d)	54.7 (d)	57.0 (d)	55.8 (d)
10	39.6 (s)	39.4 (s)	39.3 (s)	39.7 (s)
11	17.0 (t)	16.8 (t)	18.7 (t)	16.9 (t)
12	26.3 (t)	26.1 (t)	27.9 (t)	26.2 (t)
13	46.1 (d)	46.0 (d)	40.1 (d)	46.1 (d)
14	40.4 (t)	39.2 (t)	40.6 (t)	40.9 (t)
15	51.1 (t)	51.1 (t)	42.7 (t)	51.2 (t)
16	89.1 (s)	89.0 (s)	46.9 (d)	89.1 (s)
17	170.5 (s)	170.4 (s)	176.9 (s)	171.3 (s)
18	28.8 (q)	24.1 (q)	28.0 (q)	22.6 (q)
19	184.0 (d)	205.7 (d)	64.1 (t)	16.8 (q)
20	15.4 (q)	16.3 (q)	18.4 (q)	
$OCOCH_3$	171.0 (s)	170.8 (s)		170.8 (s)
$OCOCH_3$	21.1 (q)	21.0 (q)		21.0 (q)
$COOCH_3$	52.2 (q)	52.1 (q)		52.1 (q)

deposited in the Graduate Institute of Natural Products, Kaohsiung Medical University, Kaohsiung, Taiwan.

Extraction and Isolation. The air-dried stems (20 kg) of *A. glabra* L. were extracted repeatedly with MeOH at room temperature. The combined MeOH extracts were evaporated and partitioned to yield $CHCl_3$ and aqueous layers. The bases in the $CHCl_3$ solution were extracted with 3% HCl to yield the $CHCl_3$ layer and the HCl-solution layer. The $CHCl_3$ layer was dried and evaporated to leave a brownish viscous residue (200 g). The residue was further separated by column chromatography on Si gel with gradient systems of *n*-hexane−EtOAc (*n*-hexane−EtOAc 4:1 to EtOAc) and EtOAc−acetone (EtOAc to EtOAc−acetone 4:1) to yield 100 fractions of 120 mL each, which were further combined into 10 fractions according to their TLC patterns. Each fraction was rechromatographed over Si gel and purified by further Si gel column chromatography, recrystallization, or preparative TLC to yield 17 compounds. The yield amount and TLC data of these compounds are shown as follows: **1** (25.0 mg; $CHCl_3$, R_f 0.70), **2** (24.2 mg; $CHCl_3$, R_f 0.67), **3** (7.3 mg; $CHCl_3$−MeOH 10:1, R_f 0.45), **4** (10.3 mg; $CHCl_3$, R_f 0.53), **5** (15.4 mg; $CHCl_3$, R_f 0.45), **6** (25.1 mg; $CHCl_3$, R_f 0.68), 16α-hydroxy-*ent*-kauran-19-oic acid (22.9 mg; $CHCl_3$, R_f 0.41), 16*β*,17-dihydroxy-*ent*-kauran-19-oic acid (34.5 mg; $CHCl_3$, R_f 0.42), 16*β*,17-diacetoxy-*ent*-kauran-19-oic acid (55.2 mg; $CHCl_3$, R_f 0.53), 16α-hydro-*ent*-kauran-17,19-dioic acid (22.4 mg; $CHCl_3$−MeOH 10:1, R_f 0.50), *ent*-kaur-16-en-19-oic acid (15.2 mg; $CHCl_3$, R_f 0.73), 16α-hydro-19-al-*ent*-kauran-17-oic acid (320.6 mg; $CHCl_3$, R_f 0.52), 16α-hydro-19-al-*ent*-kauran-17-methyl ester (11.1 mg; $CHCl_3$, R_f 0.55), 16α-hydro-*ent*-kauran-17-oic acid (215.7 mg; $CHCl_3$, R_f 0.60), *ent*-kaur-15-en-17-ol-19-oic acid (30.4 mg; $CHCl_3$−MeOH 10:1, R_f 0.42), *ent*-kaur-15-en-17,19-diol (15.3 mg; $CHCl_3$−MeOH 10:1, R_f 0.25), and 19-nor-*ent*-kauran-4α-ol-17-oic acid (10.1 mg; $CHCl_3$−MeOH 4:1, R_f 0.38).

Annoglabasin C (16α-acetoxy-*ent*-kauran-19-oic acid-17-methyl ester) (1): white powder; mp 215−217 °C; $[\alpha]^{25}_D$ −141.0° (*c* 0.18, $CHCl_3$); IR (KBr) ν_{max} 3300, 1745, 1690, 1456, 1271 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 3.71 (3H, s, $COOCH_3$), 2.74 (1H, dd, J = 15.6, 1.6 Hz, H-15), 2.37 (1H, br s, H-13), 2.04 (3H, s, $OCOCH_3$), 1.23 (3H, s, H-18), 0.92 (3H, s, H-20); ^{13}C NMR ($CDCl_3$, 100 MHz), see Table 1; EIMS (70 eV) *m/z* 375 (8), 347 (80), 314 (100), 300 (36), 121 (96), 109 (75), 91 (80); HRFABMS *m/z* $[M + 1]^+$ 407.2451 (calcd for $C_{23}H_{35}O_6$, 407.2434).

Annoglabasin D (16α-acetoxy-*ent*-kauran-19-al-17-methyl ester) (2): white powder; mp 138−140 °C; $[\alpha]^{25}_D$ −68.3° (*c* 0.09, $CHCl_3$); IR (KBr) ν_{max} 2934, 1747, 1715, 1452, 1375, 1267 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.69 (1H, d, J = 1.2 Hz, H-19), 3.66 (3H, s, $COOCH_3$), 2.75 (1H, dd, J = 15.6, 1.6 Hz, H-15), 2.37 (1H, br s, H-13), 1.99 (3H, s, $OCOCH_3$), 0.94 (3H, s, H-18), 0.80 (3H, s, H-20); ^{13}C NMR ($CDCl_3$, 100 MHz), see Table 1; EIMS (70 eV) *m/z* 331 (12), 300 (9), 272 (3), 233 (17), 123 (23), 109 (32), 91 (44); HRFABMS *m/z* $[M + 1]^+$ 391.2477 (calcd for $C_{23}H_{35}O_5$, 391.2484).

Annoglabasin E (16α-hydro-19-ol-*ent*-kauran-17-oic acid) (3): white powder; mp 206−207 °C; $[\alpha]^{25}_D$ −53.6° (*c* 0.05, $CHCl_3$ + MeOH); IR (KBr) ν_{max} 3480, 3300, 2940, 2370, 1725, 1230, 1030 cm^{-1}; ^1H NMR (C_5D_5N, 400 MHz) δ 4.04 (1H, d, J = 10.5 Hz, H-19a), 3.67 (1H, d, J = 10.5 Hz, H-19b), 3.17 (1H, dt, J = 12.0, 6.4 Hz, H-16), 2.73 (1H, br s, H-13), 1.20 (3H, s, H-18), 0.99 (3H, s, H-20); ^{13}C NMR (C_5D_5N, 100 MHz), see Table 1; EIMS (70 eV) *m/z* 289 (100), 271 (3), 243 (5), 192 (21), 123 (87), 109 (63), 107 (32), 91 (46); HRFABMS *m/z* $[M + 1]^+$ 321.2415 (calcd for $C_{20}H_{33}O_3$, 321.2430).

Annoglabasin F (16α-acetoxy-19-nor-*ent*-kauran-4α-ol-17-methyl ester) (4): white powder; mp 164−165 °C; $[\alpha]^{25}_D$ −64.5° (*c* 0.09, $CHCl_3$); IR (KBr) ν_{max} 3400, 3300, 2940, 1745, 1690, 1220 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 3.71 (3H, s, $COOCH_3$), 2.79 (1H, dd, J = 15.6, 1.6 Hz, H-15), 2.39 (1H, br s, H-13), 2.03 (3H, s, $OCOCH_3$), 1.10 (3H, s, H-18), 0.95 (3H, s, H-19); ^{13}C NMR ($CDCl_3$, 100 MHz), see Table 1; EIMS (70 eV) *m/z* 361 (11), 302 (5), 271 (43), 243 (12), 105 (40), 91(34); HRFABMS *m/z* $[M + 1]^+$ 379.2489 (calcd for $C_{22}H_{35}O_5$, 379.2484).

16α-Methoxy-*ent*-kauran-19-oic acid (5): white powder; mp 216−219 °C; $[\alpha]^{25}_D$ −115.1° (*c* 0.16, $CHCl_3$); IR (KBr) ν_{max} 3300, 2950, 1733, 1460 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 3.12 (3H, s, OCH_3), 1.27 (3H, s, H-17), 1.22 (3H, s, H-18), 0.94 (3H, s, H-20); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 42.1 (C-1, t), 19.1 (C-2, t), 37.1 (C-3, t), 44.7 (C-4, s), 56.9 (C-5, d), 22.1 (C-6, t), 40.7 (C-7, t), 43.7 (C-8, s), 56.0 (C-9, d), 39.7 (C-10, s), 18.5 (C-11, t), 26.7 (C-12, t), 43.3 (C-13, d), 37.9 (C-14, t), 54.6 (C-15, t), 84.1 (C-16, s), 18.3 (C-17, q), 28.9 (C-18, q), 183.7 (C-19, s), 15.5 (C-20, q), 54.6 (OCH_3, s); EIMS (70 eV) *m/z* 334 ($[M]^+$, 2), 303 (21), 287 (79), 123 (64), 121 (81), 109 (89), 91 (31).

16α-Hydro-*ent*-kauran-17,19-dimethyl ester (6): white powder; mp 165−166 °C; $[\alpha]^{25}_D$ −208.2° (*c* 0.15, $CHCl_3$); IR (KBr) ν_{max} 2930, 1732, 1447, 1220 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 3.63 (3H, s, OCH_3), 3.58 (3H, s, OCH_3), 2.83 (1H, dt, J = 12.1, 6.2 Hz, H-16), 2.47 (1H, br s, H-13), 1.11 (3H, s, H-18), 0.75 (3H, s, H-20); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 40.3 (C-1, t), 18.8 (C-2, t), 37.8 (C-3, t), 44.1 (C-4, s), 56.7 (C-5, d), 21.9 (C-6, t), 39.4 (C-7, t), 43.5 (C-8, s), 55.9 (C-9, d), 39.1 (C-10, s), 17.8 (C-11, t), 27.3 (C-12, t), 47.5 (C-13, d), 41.4 (C-14, t), 41.5 (C-15, t), 45.2 (C-16, d), 175.4 (C-17, s), 28.5 (C-18, q), 178.2 (C-19, s), 15.0 (C-20, q), 51.2 (OCH_3, s), 50.9 (OCH_3, s); EIMS (70 eV) *m/z* 362 ($[M]^+$, 6), 330 (13), 303 (65), 123 (100), 121 (45), 109 (64), 91 (24).

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