Anti-inflammatory Phloroglucinols and Terpenoids from *Garcinia subelliptica*

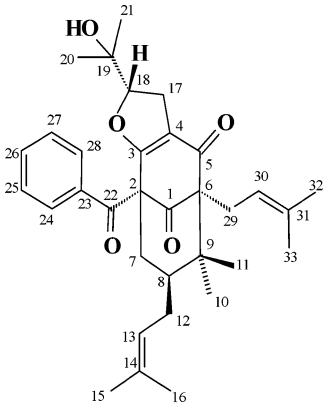
Jing-Ru Weng,[†] Lo-Ti Tsao,[‡] Jih-Pyang Wang,[‡] Ru-Rong Wu,[§] and Chun-Nan Lin*,[†]

School of Pharmacy, Kaohsiung Medical University, Kaohsiung, Taiwan 807, Republic of China, Department of Education and Research, Taichung Veterans General Hospital, Taichung, Taiwan 407, Republic of China, and Instrumental Center, National Cheng Kung University, Tainan, Taiwan 701, Republic of China

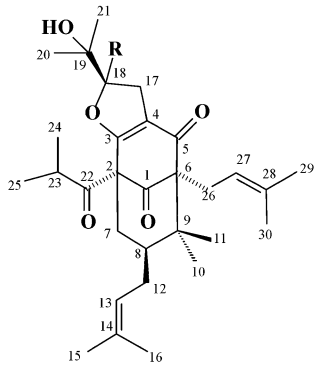
Received June 4, 2004

Three new phloroglucinols, garcinielliptones K (1), L (**2**), and M (**3**), and two new terpenoids, garcinielliptones N (**4**) and O (**5**), have been isolated from the seeds of *Garcinia subelliptica*. The structures of **1**−**5** including their relative configurations were elucidated by spectroscopic methods and supported by computer-generated molecular modeling. Compounds **2** and **3** showed potent inhibitory effects on the release of β-glucuronidase, and on β-glucuronidase and histamine, respectively, from peritoneal mast cells stimulated with *p*-methoxy-*N*-methylphenethylamine (compound 48/80) in a concentration-dependent manner. Compounds **2** and **3** showed potent effects on NO production in culture media of RAW 264.7 cells in response to lipopolysaccharide (LPS). Compound **2** also showed a potent effect on NO production in culture media of N9 cells in response to LPS/interferon-γ (IFN-γ).

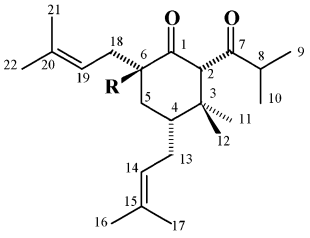
The isolation and characterization of several constituents including some antioxidant xanthones of the wood and root bark of *Garcinia subelliptica* Merr. (Guttiferae) have been reported.[1,2] In the search for bioactive constituents of Guttiferae species, the anti-inflammatory constituents of the seeds of *G. subelliptica* were investigated, and several new phloroglucinol and terpenoid derivatives have been proved to occur.[3−6] Further investigation of the constituents of the seeds of *G. subelliptica* has yielded three new phloroglucinol derivatives (**1**−**3**) and two new terpenoids (**4**, **5**). In the present paper, the structure elucidation of these five new compounds and the potential anti-inflammatory effects of **2**−**5** are reported. Insufficient amounts of compound **1** were obtained for biological testing.



1



2 R = H (α)
3 R = H (β)



4 R = H
5 R = $\underset{23}{\text{COOCH}_3}$ $\underset{24}{}$

Results and Discussion

The molecular formula of **1** was determined to be $C_{33}H_{42}O_5$ by HREIMS (*m/z* 518.3033 $[M]^+$). The IR spectrum of **1** implied the presence of OH (3440 cm^{-1}), carbonyl (1720 cm^{-1}), conjugated carbonyl (1698 cm^{-1}), and aromatic ring (1623 cm^{-1}) moieties. The ^1H NMR spectrum of **1** was similar to that of methyl nemorosone[7] except for the absence of signals due to a prenyl group and a methoxy group and the appearance of signals due to a 2-(2′-hydroxyisopropyl)-2,3-dihydrofuran ring moiety. The observed ^1H–^1H COSY correlations of H_2-17/H-18 and the HMBC correlations of H_2-17/C-3 and C-4 established the placement of the furan ring moiety. The HMBC correlations of H_2-17/C-18 and C-19, Me-20/C-18 and C-19, and Me-21/C-18 and C-19 confirmed that the hydroxyisopropyl group should be located at C-18 in **1**. The ^{13}C NMR chemical shift values of **1** (Table 1) were similar to the corresponding data of methyl nemorosone,[7] except for C-3, C-4, and C-17−C-21. Thus, **1** was characterized as having a bicyclo[3.3.1]-nonane moiety. The presence of significant peaks at *m/z* 463 $[M - a]^+$, 381 $[450 - Me - a + H]^+$, 363 $[450 - b - 1]^+$, and 327 $[M - b - c]^+$ in its EIMS also supported structure **1** (Figure S1, Supporting Information).

A NOESY experiment on **1** showed cross-peaks between H_α-7/H-8, Me-10/H_α-7, Me-10/Me-33, H_2-17/H-18 and Me-

* To whom correspondence should be addressed. Tel: +886 7 3121101, ext. 2163. Fax: +886 7 5562365. E-mail: lincna@cc.kmu.edu.tw.
† Kaohsiung Medical University.
‡ Taichung Veterans General Hospital.
§ Cheng Kung University.

10.1021/np049811x CCC: $27.50
Published on Web 10/02/2004

Table 1. ^{1}H and ^{13}C NMR Data of Compounds **1** and **2** in $CDCl_3$

	1				**2**			
		δ_H	δ_C	HMBC		δ_H	δ_C	HMBC
1			206.9	1.43 (H_α-7), 1.98 (H_β-7)			205.9	1.85 (H_β-7), 2.45 (H_2-26)
2			65.3	1.43 (H_α-7), 1.98 (H_β-7)			64.2	1.36 (H_α-7)1.85 (H_β-7), 2.45 (H-23)
3			171.9	2.94 (H_2-17)			171.7	1.85 (H_β-7), 2.97 (H_2-27)
4			118.5	2.94 (H_2-17)			120.4	2.97 (H_2-27)
5			190.3				190.5	
6			70.3	1.24 (Me-11), 1.34 (Me-10)			73.7	1.09 (Me-11), 1.23 (Me-10)
7	α	1.43 (m)	41.7		α	1.36 (m)	40.2	2.06 (H_β-12)
	β	1.98 (dd, 13.6, 4.0)			*β*	1.85 (dd, 13.6, 4.4)		
8		1.63 (m)	43.1	1.24 (Me-11), 1.34 (Me-10)		1.51 (m)	43.2	1.09 (Me-11), 1.23 (Me-10)
9			47.0	1.24 (Me-11), 1.34 (Me-10), 1.98 (H_β-7)			45.2	1.09 (Me-11), 1.23 (Me-10), 1.85 (H_β-7)
10		1.34 (s)	24.1	1.24 (Me-11)		1.09 (s)	15.7	1.23 (Me-10)
11		1.24 (s)	15.7	1.34 (Me-10)		1.23 (s)	23.9	1.09 (Me-11)
12	α	1.70 (m)	27.7		α	1.60 (m)	27.6	
	β	2.11 (dd, 13.6, 4.0)			*β*	2.06 (m)		
13		4.94 (t, 7.6)	122.3	1.56 (Me-15), 1.68 (Me-16)		4.92 (t, 7.2)	122.3	1.54 (Me-15), 1.65 (Me-16)
14			133.5	1.56 (Me-15), 1.68 (Me-16)			133.4	1.54 (Me-15), 1.65 (Me-16)
15		1.56 (s)	17.9	1.68 (Me-16)		1.54 (s)	17.9	
16		1.68 (s)	26.0	1.56 (Me-15)		1.65 (s)	25.9	1.54 (Me-15)
17		2.94 (2H, d, 10.0)	26.5			2.97 (d, 10.4)	26.7	
18	*β*	4.65 (t, 10.0)	93.5	0.90 (Me-20), 0.90 (Me-21), 2.94 (H_2-17)		4.79 (t, 10.4)	94.0	1.24 (Me-21), 1.38 (Me-20), 2.97 (H_2-17)
19			70.6	0.90 (Me-20), 0.90 (Me-21), 2.94 (H_2-17)			71.1	1.24 (Me-21), 1.38 (Me-20), 2.97 (H_2-17)
20		0.90 (s)	26.4	0.90 (Me-21)		1.38 (s)	26.7	1.24 (Me-21)
21		0.90 (s)	23.7	0.90 (Me-20)		1.24 (s)	25.2	
22			192.6	1.43 (H_α-7), 7.57 (H-24 and H-28)			208.4	1.13 (Me-24), 1.16 (Me-25), 2.45 (H-23)
23			137.1	7.35 (H-25 and H-27)		2.45 (m)	40.7	1.13 (Me-24), 1.16 (Me-25)
24		7.57 (m)	128.2	7.35 (H-25 and H-27)		1.13 (d, 6.4)	20.9	1.16 (Me-25)
25		7.35 (m)	128.5	7.50 (H-26)		1.16 (d, 6.4)	21.0	1.13 (Me-24)
26		7.50 (m)	132.8	7.57 (H-24 and H-28)		2.45 (m)	29.2	
27		7.35 (m)	128.5			5.00 (t, 7.2)	119.5	1.65 (Me-30), 1.67 (Me-29), 2.45 (H_2-26)
28		7.57 (m)	128.2	7.34 (H-26 and H-27)			134.1	1.65 (Me-30), 1.67 (Me-29)
29	α	2.47 (dd, 14.0, 7.6)	29.3			1.67 (s)	18.0	1.65 (Me-30)
	β	2.58 (dd, 14.0, 7.6)						
30		5.06 (t, 7.6)	119.5	1.68 (Me-33), 1.70 (Me-32)		1.65 (s)	25.9	1.67 (Me-29)
31			134.7	1.68 (Me-33), 1.70 (Me-32)				
32		1.70 (s)	25.9	1.68 (Me-33)				
33		1.68 (s)	18.2	1.68 (Me-33)				

21, Me-20/H-28, and H-28/H_α-7. The above result suggested that the prenyl groups at C-6, the benzoyl group at C-2, the 2-hydroxyisopropyl unit, and the hydrogen group at C-8 are on the α side of **1**. From the ^{1}H NMR, COSY, and NOESY spectra, a computer-generated 3D structure of **1** was obtained by using the molecular modeling program CS CHEM 3D V 3.5.1, with MM2 force-field calculations for energy minimization (Figure S2, Supporting Information). The calculated distances between H_α-7/H-8 (3.098 Å), Me-10/H_α-7 (3.770 Å), Me-10/Me-33 (2.751 Å), H_2-17/H-18 (2.354 Å), H_2-17/Me-21 (3.020 Å), Me-20/H-28 (3.228 Å), and H-7$_\alpha$/H-28 (2.369 Å) are all less than 4.00 Å. This is consistent with the well-defined NOESY interactions observed for each of these proton pairs. Thus, garcinielliptone K was characterized as 2α-benzoyl-9,9-dimethyl-6α,8*β*-di(*γ*,*γ*-dimethylallyl)-3,4-[2α-(2′-hydroxyisopropyl)-2,3-dihydrofuran]-8α-*H-cis*-bicyclo[3.3.1]nona-3-ene-1,5-dione (**1**).

Compound **2** showed the same molecular formula and an IR spectrum similar to **1**. The ^{1}H NMR spectrum of **2** was very similar to that of **1** except for the absence of signals due to a benzoyl group and the appearance of signals due to a 1-oxo-2-methylpropyl group. The ^{1}H-^{1}H COSY correlations of H-23/Me-24 and Me-25 and the HMBC correlations of H-23/C-2 and C-22 confirmed that the 1-oxo-2-methylpropyl group was linked to C-2. In the ^{13}C NMR spectrum of **2** (Table 1), the chemical shift values of **2** were very similar to the corresponding data of **1** except for C-22−C-25. Significant peaks exhibited in the EIMS of **2** (Figure S1, Supporting Information) also supported the structure proposed for **2**. Thus, garcinielliptone L (**2**) was characterized with a bicyclo[3.3.1]nonane skeleton.

The relative configurations at C-2, C-6, C-8, and C-18 were determined as shown in **2** from the results of a NOESY experiment (Figure S2, Supporting Information). The calculated distances between each of these proton pairs in the 3D structure of **2** (Figure S2, Supporting Information), obtained as described for **1**, were all less than 4.00 Å except for Me-10/Me-29 (4.094 Å). This is consistent with the well-defined NOESY interaction observed for each of these proton pairs. Thus, garcinielliptone L was characterized as 9,9-dimethyl-6α,8*β*-di(*γ*,*γ*-dimethylallyl)-3,4-[2*β*-(2′-hydroxyisopropyl)-2,3-dihydrofuran]-2α-(1-oxo-2-methylpropyl)-8α-*H-cis*-bicyclo[3.3.1]nona-1,5-dione (**2**).

The molecular formula of **3** was determined to be $C_{30}H_{44}O_5$ by HREIMS (*m*/*z* 484.3197 $[M]^+$). The IR spectrum of **3** implied the presence of OH (3432 cm^{-1}), carbonyl (1724 cm^{-1}), conjugated carbonyl (1646 cm^{-1}), and C=C (1617 cm^{-1}) moieties. The ^{1}H and ^{13}C NMR spectra of **3** (see Experimental Section) resembled those of **2** except that the H-18 signal was shifted upfield compared to that of the

corresponding proton signal of **2**, and the optical rotation was also different. The relative configuations at C-2, C-6, and C-8 were determined by comparison with the original stereochemistry determined for **2**. The NOESY experiment of **3** showed a cross-peak between H_β-17/Me-21 and Me-21/H-18. On the basis of a NOESY experiment, the 2-hydroxyisopropyl group and the proton at C-18 were both on the β side of **3**. Thus, garcinielliptone M was characterized as 9,9-dimethyl-6α,8β-di(γ,γ-dimethylallyl)-3,4-[2β-(2′-hydroxyisopropyl)-2,3-dihydrofuran]-2α-(1-oxo-2-methylpropyl)-8α-*H-cis*-bicyclo[3.3.1]nona-1,5-dione (**3**).

Compound **4** exhibited a molecular formula of $C_{22}H_{36}O_2$ as determined by HRFABMS (*m/z* 333.2788 $[M + 1]^+$). The IR spectrum of **4** showed carbonyl (1724, 1698 cm^{-1}) moieties. The ^1H NMR spectrum of **4** (see Experimental Section) was closely comparable to that of (2*R*,3*R*,4*S*,6*S*)-3-methyl-4,6-di(3-methyl-2-butenyl)-3-(4-methyl-3-pentenyl)-cyclohexanone[8] except for the absence of signals due to a 2-methyl-2-pentenyl group and the appearance of signals due to an additional tertiary methyl group. The HMBC correlations of H-2/C-1, C-11, and C-12 established the placement of the 2-methyl-1-oxopropyl group at C-2, and the NOESY correlation of H-2/Me-12 confirmed that the tertiary methyl group was located at C-3.

The NOESY experiment of **4** showed selected cross-peaks as shown in a 3D drawing (Figure S2, Supporting Information). The relative configurations at C-2, C-4, and C-6 were deduced from the NOESY cross-peaks of H_α-5/H_α-18, H-6/H-2, H-6/H_β-5, H_α-5/Me-17, and H-2/H-4. The prenyl groups at C-4 and C-6 and the 1-oxo-2-methylpropyl group at C-2 were all determined on the α side of **4**. Based on the information from the ^1H NMR, COSY, and NOESY spectra, a computer-generated 3D structure was obtained by using the above-mentioned molecular modeling program with MM2 force-field calculations for energy minimization (Figure S2, Supporting Information). The calculated distances between H_α-5/H_α-18 (3.308 Å), H_α-5/Me-17 (2.870 Å), H_β-5/H-6 (2.382 Å), and H_β-2/H_β-4 (2.529 Å) were all less than 4.00 Å. This is consistent with the well-defined NOESY interaction observed for each of these proton pairs. Thus, garcinielliptone N was characterized as 3,3-dimethyl-4α,6α-di(γ,γ-dimethylallyl)-2α-(2-methyl-1-oxopropyl)cyclohexanone (**4**).

The molecular formula $C_{24}H_{38}O_4$ of **5** was established by HREIMS (*m/z* 390.2777 $[M]^+$). The IR spectrum of **5** indicated the presence of a carbonyl (1724 cm^{-1}) moiety. The ^1H NMR spectrum of **5** (see Experimental Section) was very similar to that of **4** except for the appearance of a methoxycarbonyl group. The ^{13}C NMR spectrum revealed 24 carbon signals, which included eight methyls, one methoxyl, three methylenes, three methines, two olefinic carbons, three carbonyls, and four other quaternary carbons. The structure of **5** was deduced by analysis of its HMQC and HMBC spectra and by comparison with **4**. The relative configurations at C-2, C-4, and C-6 are determined by comparing the relative stereochemistry of **4**. Thus, garcinielliptone O was characterized as 6-methoxylcarbonyl-3,3-dimethyl-4α,6α-di(γ,γ-dimethylallyl)-2α-(2-methyl-1-oxo-propyl)cyclohexanone (**5**).

The in vitro anti-inflammatory activities of **2**−**5** were studied by measuring the inhibitory effects on chemical mediator release from mast cells, neutrophils, macrophages, and microglial cells. Insufficient amounts of compound **1** were obtained for biological testing. Compounds **2** and **3** showed potent inhibitory effects on the release of β-glucuronidase, and β-glucuronidase and histamine, respectively, from rat peritoneal mast cells stimulated with compound 48/80 (10 μg /mL) in a concentration-dependent manner, respectively, while **4** and **5** had no inhibitory effects observed in the concentration range used (Table 2). These results indicated that triterpenoids such as **2** or **3** with a bicyclo[3.3.1]nonane moiety did show significant inhibitory effects, and the inhibitory effects of **3** were more potent than that of mepacrine, a positive control used in this experiment. As shown in Table 2, this clearly indicates that a β-H at C-18 (i.e., in **3**) enhances the inhibitory effects on rat mast cell degranulation.

Table 2. Inhibitory Effects of Compounds **2**−**5** on the Release of β-Glucuronidase and Histamine from Rat Mast Cells Stimulated with Compound 48/80 (10 μg/mL)

	IC_{50} (μM)[a]	
compound	β-glucuronidase	histamine
2	22.9 ± 2.4	>30 (38.1 ± 2.8)
3	13.6 ± 2.0	19.0 ± 2.0
4	>30 (30.2 ± 4.3)	>30 (13.7 ± 3.6)
5	>30 (43.9 ± 6.7)	>30 (32.8 ± 14.1)
mepacrine[b]	13.7 ± 3.2	23.3 ± 3.0

[a] When 50% inhibition could not be reached at the highest concentration, the % of inhibition is given in parentheses. Data are presented as means ± SEM (n = 3−5). [b] Mepacrine was used as a positive control.

Table 3. Inhibitory Effects of Compounds **2**−**5** on the Accumulation of NO_2^- in the Culture Media of RAW 264.7 Cells in Response to LPS (1 μg mL^{-1}) and N9 Cells in Response to LPS (10 ng/mL)/IFN-γ (10 U/mL)

	IC_{50} (μM)[a]	
compound	RAW 264.7 cells	N9 cells
2	22.7 ± 1.5	12.8 ± 0.8
3	15.3 ± 1.9	>30 (9.0 ± 3.8)
4	>30 (5.7 ± 0.5)	>30 (34.5 ± 2.8)
5	>30 (22.1 ± 1.8)	>30 (34.6 ± 2.6)
1400W[b]	2.9 ± 0.1	6.3 ± 0.8

[a] When 50% inhibition could not be reached at the highest concentration, the % of inhibition is given in parentheses. Data are presented as means ± SEM (n = 3−5). [b] *N*-(3-Aminomethyl-)benzylacetamidine (1400W).

Compounds **2**−**5** did not cause a significant inhibition of neutrophil degranulation stimulated with formyl-Met-Leu-Phe (fMLP) (1 μM)/cytochalasin (CB) (5 μg/mL) and the superoxide anion generation in rat neutrophils stimulated with fMLP (0.3 μM)/CB (5 μg/mL) or phorbol myristate acetate (PMA) (3 nM) (data not shown). Compounds **2** and **3** evoked a concentration-dependent induced superoxide anion generation in rat neutrophils stimulated with fMLP (0.3 μM)/CB (5 μg/mL). The maximum response was observed at 3−30 μM. These data indicated that **2** and **3** may induce a respiratory burst in rat neutrophils.

Treatment of RAW 264.7 macrophage-like cells with LPS (1 μg/mL) or N9 microglial cells with LPS (10 ng/mL)/IFN-γ (10 U/mL) for 24 h induced NO production, as assessed by measuring the accumulation of nitrite, a stable metabolite of NO, in the media, based on the Griess reaction. As shown in Table 3, compounds **2** and **3** produced significant inhibition of NO_2^- accumulation in RAW 264.7 cell culture medium in response to LPS (1 μg/mL). Compound **2** also showed potent inhibitory effects on NO_2^- accumulation in N9 cell culture medium in response to LPS (10 ng/mL)/IFN-γ (10 U/mL). Table 3 clearly indicates that an α-H at C-18 (i.e., in **2**) enhances the inhibitory effects on NO_2^- accumulation in RAW 264.7 and N9 cell culture media in response to LPS and LPS/IFN-γ, respectively. Compounds **2** and **3** (each at 30 μM) showed slight inhibitory effects on tumor-necrosis factor-α (TNF-α) production in RAW

264.7 cell culture medium in response to LPS with % inhibitions of 32.1 ± 10.9 and 36.9 ± 9.8 μM, respectively. The present study demonstrated that the effects of **2** and **3** on mast cell degranulation, NO production in macrophages and microglial cells, and TNF-α production in macrophages may have therapeutic potential in the treatment or prevention of central and peripheral inflammatory disease.

Experimental Section

General Experimental Procedures. Optical rotations were obtained on a JASCO model DIP-370 digital polarimeter. UV spectra were obtained on a JASCO model UV−vis spectrophotometer. IR spectra were recorded on a Hitachi model 260-30 spectrophotometer. ^{1}H (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Varian Unity-400 spectrometer. MS were obtained on a JMS-HX100 mass spectrometer.

Plant Material. The seeds of *G. subelliptica* were collected at Kaohsiung, Taiwan, in July 2001. A voucher specimen (2001-3) has been deposited at the Department of Medicinal Chemistry, School of Pharmacy, Kaohsiung Medical University.

Extraction and Isolation. The fresh seeds (7.5 kg) obtained from the fresh fruits (22.8 kg) of *G. subelliptica* were extracted with $CHCl_3$ at room temperature. The $CHCl_3$ extract was concentrated under reduced pressure to afford a brown residue (130 g). The residue (130 g) was fractionated by chromatography over silica gel, using *n*-C_6H_{12}−EtOAc (19:1), *n*-C_6H_{12}−EtOAc (9:1), *n*-C_6H_{12}−EtOAc−MeOH (4:1:1), and *n*-C_6H_{12}−EtOAc−MeOH (1:2:1), to afford fractions A, B, C, and D. Fraction C was rechromatographed over silica gel, and elution with CH_2Cl_2−EtOAc (19:1) yielded **1** (2 mg). Fraction D was rechromatographed over silica gel, and elution with $CHCl_3$−acetone (19:1) yielded **2** (8 mg) and **3** (6 mg). Fraction B was further purified by chromatography over silica gel, using *n*-C_6H_{12}−EtOAc (10:1), to afford fractions B_1 and B_2. Fraction B_2 was rechromatographed over silica gel, and elution with *n*-C_6H_{12}−EtOAc (16:1) yielded **4** (4 mg) and **5** (18 mg). Fraction C was also further fractionated by chromatography over silica gel, using *n*-C_6H_{12}−acetone, (4:1) to afford fractions C_1 and C_2. Fraction C_2 was rechromatographed over silica gel, and elution with $CHCl_3$−EtOAc (9:1) yielded **5** (3 mg). Compounds **1**−**5** were purified by flash column chromatography on silica gel.

Garcinielliptone K (1): colorless oil; [α] +27° (*c* 0.27, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 280 (4.11) nm; IR (NaCl) ν_{max} 3440, 1720, 1698, 1623 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz), see Table 1; EIMS *m/z* 518 $[M]^+$ (35), 463 (5), 450 (21), 381 (68), 364 (6), 327 (100), 268 (30), 105 (52); HREIMS *m/z* $[M]^+$ 518.3033 (calcd for $C_{33}H_{42}O_5$, 518.3032).

Garcinielliptone L (2): colorless oil; [α] −41° (*c* 0.29, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 270 (4.00) nm; IR (NaCl) ν_{max} 3446, 1720, 1646, 1617 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz), see Table 1; EIMS *m/z* 484 $[M]^+$ (30), 469 (8), 441 (17), 413 (13), 373 (95), 347 (90), 293 (100), 275 (25); HREIMS *m/z* $[M]^+$ 484.3200 (calcd for $C_{30}H_{44}O_5$, 484.3188).

Garcinielliptone M (3): colorless oil; [α] +73° (*c* 0.16, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 280 (4.10) nm; IR (NaCl) ν_{max} 3432, 1724, 1646, 1617 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.03 (3H, d, J = 6.4 Hz, Me-24), 1.05 (3H, s, Me-10), 1.15 (3H, d, J = 6.4 Hz, Me-25), 1.25 (3H, s, Me-11), 1.28 (3H, s, Me-21), 1.32 (3H, s, Me-20), 1.34 (1H, m, H_α-7), 1.50 (3H, s, Me-15), 1.51 (1H, m, H-8), 1.59 (1H, m, H-12), 1.64 (3H, s, Me-16), 1.65 (6H, s, Me-29 and -30), 1.83 (1H, dd, J = 13.6, 4.3 Hz, H_β-7), 2.05 (1H, m, H-12), 2.42 (1H, m, H-23), 2.42 (2H, m, H_2-26), 2.92 (1H, dd, J = 15.2, 10.4 Hz, H_α-17), 3.02 (1H, dd, J = 15.2, 10.4 Hz, H_β-17), 4.66 (1H, t, J = 10.4 Hz, H-18), 4.89 (1H, t, J = 7.2 H z, H-13), 5.00 (1H, t, J = 7.2 Hz, H-27); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.7 (C-10), 17.8 (C-15), 18.0 (C-29), 20.5 (C-24), 20.8 (C-25), 24.1 (C-11), 25.8 (C-16), 26.1 (C-20), 25.0 (C-21), 25.9 (C-30), 26.8 (C-17), 27.5 (C-12), 29.2 (C-26), 40.2 (C-7), 40.7 (C-23), 43.1 (C-8), 44.9 (C-9), 63.9 (C-2), 71.3 (C-19), 73.8 (C-6), 93.0 (C-18), 119.5 (C-27), 119.9 (C-4), 122.3 (C-13), 133.3 (C-14), 134.1 (C-28), 171.8 (C-3), 190.7 (C-5), 206.0 (C-1), 208.6 (C-22); EIMS *m/z* 484 $[M]^+$ (28), 415 (13), 373 (45), 347 (100), 293 (99), 69 (46); HREIMS *m/z* $[M]^+$ 484.3197 (calcd for $C_{30}H_{44}O_5$, 484.3188).

Garcinielliptone N (4): colorless oil; [α] −42° (*c* 0.38, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 284 (3.11) nm; IR (NaCl) ν_{max} 1724, 1698 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.99 (3H, d, J = 6.4 Hz, Me-10), 1.00 (3H, s, Me-12), 1.03 (3H, d, J = 6.4 Hz, Me-9), 1.03 (3H, s, Me-11), 1.16 (1H, d, J = 6.4 Hz, H_α-5), 1.54 (1H, m, H_β-4), 1.57 (3H, s, Me-21), 1.57 (3H, s, Me-22), 1.66 (3H, s, Me-17), 1.67 (1H, m, H_α-18), 1.70 (3H, s, Me-16), 1.91 (1H, m, H_β-18), 2.09 (1H, dd, J = 6.4, 3.6 Hz, H_β-5), 2.16 (1H, m, H_α-13), 2.35 (1H, m, H_β-13), 2.35 (1H, m, H_β-6), 2.40 (1H, m, H-8), 3.62 (1H, m, H_β-2), 5.05 (1H, t, J = 8.0 Hz, H-19), 5.10 (1H, t, J = 8.0 Hz, H-14); ^{13}C NMR (100 MHz) δ 15.8 (C-12), 17.2 (C-11), 17.7 (C-21), 17.8 (C-22), 18.0 (C-10), 25.7 (C-17), 25.8 (C-16), 26.6 (C-9), 27.4 (C-13), 27.5 (C-18), 34.8 (C-5), 42.9 (C-8), 43.4 (C-3), 48.2 (C-4), 50.9 (C-6), 70.6 (C-2), 121.4 (C-19), 123.2 (C-14), 132.7 (C-15), 133.1 (C-20), 208.8 (C-1), 210.9 (C-7); FABMS *m/z* 333 $[M + 1]^+$ (7); HRFABMS *m/z* $[M]^+$ 333.2788 (calcd for $C_{22}H_{36}O_2$ 333.2793).

Garcinielliptone O (5): colorless oil; [α] −277° (*c* 016, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 280 (4.00) nm; IR (NaCl) ν_{max} 1724 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.99 (3H, s, Me-12), 1.00 (3H, d, J = 6.4 Hz, Me-10), 1.02 (3H, s, Me-11), 1.06 (3H, d, J = 6.4 Hz, Me-9), 1.28 (1H, dd, J = 14.4, 12.8 Hz, H_α-5), 1.56 (3H, s, Me-22), 1.57 (1H, m, H-8), 1.60 (3H, s, Me-17), 1.67 (1H, m, H_α-13), 1.67 (3H, s, Me-21), 1.73 (3H, s, Me-16), 2.18 (1H, dd, J = 14.4, 7.6 Hz, H_β-13), 2.28 (1H, dd, J = 14.4, 7.6 Hz, H_α-18), 2.46 (1H, m, H_β-5), 2.48 (1H, m, H_β-18), 2.51 (1H, m, H_β-4), 3.75 (3H, s, OMe-24), 5.04 (1H, t, J = 7.6 Hz, H-19), 5.13 (1H, t, J = 7.6 Hz, H-14); ^{13}C NMR (100 MHz) δ 15.6 (C-12), 17.0 (C-10), 17.8 (C-22), 17.9 (C-17), 18.1 (C-11), 25.8 (C-16), 25.9 (C-21), 26.5 (C-9), 27.4 (C-13), 33.2 (C-18), 36.7 (C-5), 42.5 (C-4), 43.4 (C-3), 45.7 (C-8), 52.4 (OMe-24), 61.4 (C-6), 69.4 (C-2), 118.1 (C-19), 122.8 (C-14), 132.9 (C-15), 135.2 (C-20), 172.2 (C-23), 203.9 (C-1), 210.2 (C-7); EIMS *m/z* 390 $[M]^+$ (100), 347 (28), 331 (59), 287 (16), 247 (24), 219 (27), 69 (42); HREIMS *m/z* $[M]^+$ 390.2777 (calcd for $C_{24}H_{38}O_4$ 390.2770).

Bioassays. Assays for inhibition of chemical mediators induced by various stimulants in mast cells, neutrophils, RAW 264.7 cells, and N9 cells were performed by the methods described previously.[9]

Acknowledgment. This work was partially supported by a grant from the National Science Council of the Republic of China (NSC 92-2320-B037-041).

Supporting Information Available: Figures showing mass spectral fragmentation patterns for **1** and **2** and selected NOESY correlations for **1**, **2**, and **4** are available free of change via the Internet at http://pubs.acs.org.

References and Notes

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NP049811X