Three New Furan Derivatives and a New Fatty Acid from a Taiwanese Marine Sponge *Plakortis simplex*

Ya-Ching Shen,*,† Chaturvedula V. S. Prakash,† and Yao-Haur Kuo‡

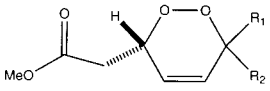
Institute of Marine Resources, National Sun Yat-sen University, 70 Lien-Hai Road, Kaohsiung, Taiwan, Republic of China, and National Research Institute of Chinese Medicine, Taipei, Taiwan, Republic of China

Received August 21, 2000

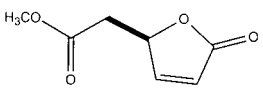
Three new furan derivatives, plakorsins A−C (**6**−**8**), together with a new fatty acid, plakortic acid (**9**), have been isolated from the Taiwanese marine sponge *Plakortis simplex* in addition to the known metabolites chondrillin (**1**), 6-*epi*-chondrillin (**2**), 2-oxo-2,5-dihydrofuran-5-acetic acid methyl ester (methyl 1,4-epoxy-1-oxo-2-hexenoate) (**3**), dimethyl *β*-ketoadipate (**4**), and the monomethyl ester of *cis*,*cis*-muconic acid (**5**). The structures of these compounds were established mainly on the basis of spectral data and chemical methods. Biological studies revealed that compound **7** exhibited cytotoxic activity against COLO-250 and KB-16 cells, and compound **1** is active against KB-16 cells.

Furan fatty acids are commonly isolated from fish lipids,[1−6] but also from a number of marine organisms such as diatoms,[7] crayfish,[8,9] ascidians, scallops, soft corals,[10] and sponges.[11,12] Reports of their isolation from plant sources are less common.[13−16] The furan fatty acid (8*Z*,11*Z*,14*Z*,17*Z*)-3,6-epoxyeicos-3,5,8,11,14,17-hexenoic acid isolated from the New Zealand sponge *Hymeniacidon huraki*[12] was responsible for the cytotoxicity of its extract (P-388; IC_{50} 13.4 *μ*g/mL), whereas the methyl and stearyl esters of the acid showed inflammatory activity.

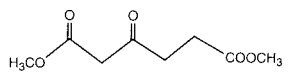
As a part of our continuing research on the isolation of bioactive substances from marine organisms, we have focused our interest on Taiwanese marine sponges.[17−19] The EtOH extract of the sponge *Plakortis simplex* Schulze (family Plakinidae) after extensive chromatography yielded nine compounds, which included chondrillin (**1**), 6-*epi*-chondrillin (**2**), 2-oxo-2,5-dihydrofuran-5-acetic acid methyl ester (**3**), dimethyl *β*-ketoadipate (**4**), the monomethyl ester of *cis*,*cis*-muconic acid (**5**), and four new compounds, out of which three (**6**−**8**) were furan derivatives and **9** was an epoxy fatty acid. In this paper we wish to report the isolation and structure elucidation of the four new compounds, plakorsins A−C (**6**−**8**) and plakortic acid (**9**).



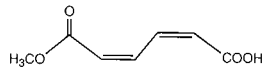
(**1**) R_1 = β-OCH_3, R_2 = α-$CH_2(CH_2)_{14}CH_3$
(**2**) R_1 = α-OCH_3, R_2 = β-$CH_2(CH_2)_{14}CH_3$



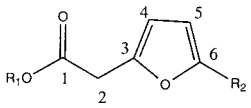
(**3**)



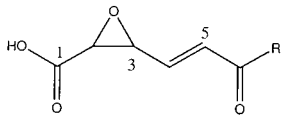
(**4**)



(**5**)



(**6**) R_1 = CH_3, R_2 = $CH_2(CH_2)_{14}CH_3$
(**7**) R_1 = H, R_2 = $CH_2(CH_2)_{14}CH_3$
(**8**) R_1 = CH_3, R_2 = $CH_2(CH_2)_6CH(CH_2CH_2CHO)(CH_2)_3CH_3$



(**9**) R = $CH_2(CH_2)_{14}CH_3$

Results and Discussion

The EtOAc soluble fraction from the alcoholic extract of *P. simplex* Schulze was repeatedly chromatographed over silica gel with solvents of increasing polarity (*n*-hexane/$CHCl_3$/MeOH mixtures) to furnish chondrillin (**1**, 0.13%), 6-*epi*-chondrillin (**2**, 4.09%), 2-oxo-2,5-dihydrofuran-5-acetic acid methyl ester (**3**, 0.115%), dimethyl *β*-ketoadipate (**4**, 0.033%), *cis*,*cis*-muconic acid methyl ester (**5**, 0.024%), plakorsins A (**6**, 0.026%), B (**7**, 0.039%), C (**8**, 0.033%), and plakortic acid (**9**, 0.024%). The structures of compounds **1**−**3** were identified by spectral data comparisons with compounds isolated from *Xestospongia* sp.[20] and *Plakortis lita*.[21] Although compounds **4** and **5** have been synthesized previously, this is the first report of their isolation from a natural source. Structures for **4** and **5** were also confirmed by comparison of spectral data with literature reports.[22,23]

Plakorsin A (**6**) was isolated as a colorless oil, and its molecular formula was deduced as $C_{23}H_{40}O_3$ from HREIMS data. The furan moiety was evident from UV (220 and 282 nm) and IR (3016, 1523, and 770 cm^{-1}) absorbances and was confirmed by a positive Ehrlich test.[24] The IR also showed the presence of an ester carbonyl group (1739 cm^{-1}), and this was supported by the ^{13}C NMR value at *δ* 170.5. The ^1H NMR spectrum of **6** (Table 1) showed the presence of two doublets at *δ* 6.09 (*J* = 3 Hz) and *δ* 5.91 (*J* = 3 Hz), a carbomethoxy singlet at *δ* 3.71, and a methylene singlet at *δ* 3.64 similar to the spectrum of the methyl ester of (8*Z*,11*Z*,14*Z*,17*Z*)-3,6-epoxyeicos-3,5,8,11,-14,17-hexenoic acid isolated from the sponge *Dictyonella insica*.[11] The ^{13}C NMR data (Table 2) of C-1−C-6 in **6** are almost identical to those of the above methyl ester. Further the ^1H NMR of **6** showed the presence of a triplet at *δ* 2.61 (*J* = 7.8 Hz), which can be attributed to the allylic methylene at C-7, as confirmed from the HMBC in Figure 1. The ^1H NMR spectrum of **6** also exhibited a multiplet at *δ* 1.63 for two protons, a broad singlet at *δ* 1.26 for 26 protons, and a triplet at *δ* 0.88 (*J* = 6.6 Hz) for three protons, suggesting the presence of a $C_{15}H_{31}$ side chain. A

* To whom correspondence should be addressed. Tel: (886) 7-525-2000 ext 5058. Fax: (886) 7-525-5020. E-mail: ycshen@mail.nsysu.edu.tw.
† National Sun Yat-sen University.
‡ National Research Institute of Chinese Medicine.

10.1021/np000413d CCC: $20.00
Published on Web 02/21/2001

Table 1. ^{1}H NMR Data for Compounds **6**−**9**[a]

position	6	7	8	9
2	3.64 (s)	3.68 (s)	3.62 (s)	3.48 (s)
3				3.74 (d, 5.4)
4	6.09 (d, 3)	6.12 (d, 3)	6.08 (d, 3)	6.46 m
5	5.91 (d, 3)	5.91 (d, 3)	5.91 (d, 3)	6.49 m
7	2.61 (t, 7.8)	2.58 (t, 7.8)	2.57 (t, 7.8)	2.55 (t, 7.8)
8	1.63 m	1.61 m	1.63 m	1.60 m
9−13	1.26 (br s)	1.26 (br s)	1.25 (br s)	1.25 (br s)
14	1.26 (br s)	1.26 (br s)	1.60 m	1.25 (br s)
15−17	1.26 (br s)	1.26 (br s)	1.25 (br s)	1.25 (br s)
18	1.26 (br s)	1.26 (br s)	0.88 (t, 6.6)	1.25 (br s)
19	1.26 (br s)	1.26 (br s)		1.25 (br s)
20	1.26 (br s)	1.26 (br s)		1.25 (br s)
21	1.26 (br s)	1.26 (br s)		1.25 (br s)
22	0.88 (t, 6.6)	0.88 (t, 6.6)		0.88 (t, 6.6)
OCH_3	3.71 (s)		3.68 (s)	
1′			1.62 m	
2′			2.55 (t, 7.8)	
3′ (CHO)			9.77 (t, 1.8)	

[a] Multiplicities and coupling constants in Hz are in parentheses; chemical shifts are given in δ.

Table 2. ^{13}C NMR Data for Compounds **6**−**9**[a]

position	6	7	8	9
1	170.5 (s)	175.8 (s)	170.1 (s)	171.9 (s)
2	34.0 (t)	33.8 (t)	34.0 (t)	54.4 (d)
3	156.2 (s)	156.5 (s)	156.2 (s)	56.4 (d)
4	108.4 (d)	108.9 (d)	108.4 (d)	133.5 (d)
5	105.4 (d)	105.5 (d)	105.4 (d)	138.9 (d)
6	145.4 (s)	145.7 (s)	145.3 (s)	199.4 (s)
7	29.2 (t)[b]	29.2 (t)[c]	29.2 (t)[d]	41.0 (t)
8	29.4 (t)[b]	29.4 (t)[c]	29.4 (t)[d]	23.8 (t)
9	28.0 (t)	28.0 (t)	28.0 (t)	29.6 (t)[e]
10	29.6 (t)[b]	29.5 (t)[c]	29.6 (t)[d]	29.6 (t)[e]
11	29.7 (t)[b]	29.6 (t)[c]	29.7 (t)[d]	29.6 (t)[e]
12	29.7 (t)[b]	29.6 (t)[c]	28.0 (t)	29.4 (t)[e]
13	29.6 (t)[b]	29.5 (t)[c]	31.9 (t)	29.4 (t)[e]
14	29.6 (t)[b]	29.5 (t)[c]	22.1 (d)	29.3(t)[e]
15	29.6 (t)[b]	29.5 (t)[c]	29.5 (t)[d]	29.4 (t)[e]
16	29.7 (t)[b]	29.6 (t)[c]	29.4 (t)	29.3 (t)[e]
17	29.7 (t)[b]	29.6 (t)[c]	22.7 (t)	29.4 (t)[e]
18	29.7 (t)[b]	29.6 (t)[c]	14.2 (q)	29.4 (t)[e]
19	29.6 (t)[b]	29.5 (t)[c]		29.6 (t)[e]
20	28.0 (t)	28.0 (t)		28.2 (t)
21	31.9 (t)	31.9 (t)		31.9 (t)
22	22.7 (t)	22.6 (t)		22.7 (t)
23	14.2 (q)	14.1 (q)		14.1 (q)
OCH_3	52.1 (q)		52.2 (q)	
1′			28.0 (t)	
2′			43.9 (t)	
CHO			202.9 (d)	

[a] s = C, d = CH, t = CH_2, q = CH_3. Multiplicities and assignments made by HSQC and HMBC. [b−e] Data may be interchangeable in the respective columns.

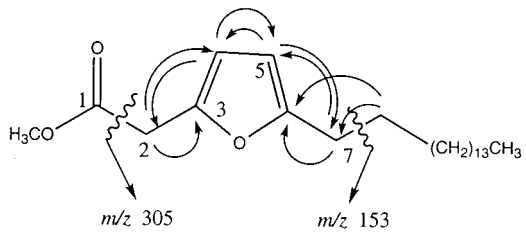


Figure 1. Selective HMBC and fragmentation of **6**.

similar side chain-containing compound, 5-hexadecylpyrrole-2-carboxaldehyde, was isolated from the marine sponge *Laxosuberites* sp.[25] The ^{1}H NMR and ^{13}C NMR values of the side chains of compound **6** and the above-mentioned pyrrole-2-carboxaldehyde are similar and confirmed the similar nature.

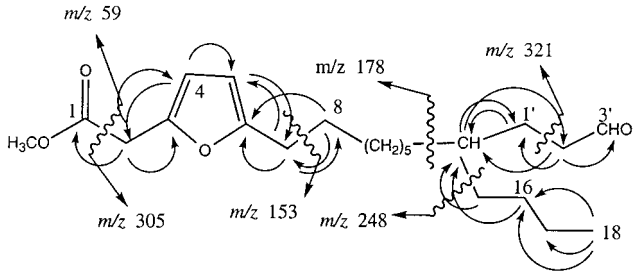


Figure 2. HMBC and fragmentation of **8**.

Plakorsin B (**7**) was isolated as an amorphous solid, whose molecular formula was established as $C_{22}H_{38}O_3$ from HREIMS analysis. Its UV (220 and 290 nm) absorption and IR bands showed the presence of the furan moiety as well as carboxylic acid (3575, 1704 cm^{-1}) instead of an ester. The ^{1}H and ^{13}C NMR spectra of **7** were very similar to those of **6**, but lacked carbomethoxy signals. The EIMS spectrum, 14 amu less than **6**, suggested that **7** might be the free acid form, which was well supported by the strong mass fragment at *m*/*z* 305 ([M − COOH]$^+$). Furthermore, compound **7** furnished a methyl ester identical to compound **6** on methylation with CH_2N_2.

Plakorsin C (**8**) was obtained as a colorless oil, and its molecular formula was deduced as $C_{22}H_{36}O_4$ from HREIMS spectra. Its UV (221 and 291 nm) and IR (3017, 1510, and 745 cm^{-1}) spectra indicated the presence of a furan moiety as in compounds **6** and **7**. Furthermore, IR and NMR, respectively, suggested the presence of an ester carbonyl (1735 cm^{-1} and δ 170.1 s) and an aliphatic aldehyde (1730 cm^{-1} and δ 202.9 d). The ^{1}H and ^{13}C NMR data of **8** (Tables 1 and 2) can be aligned with C-1−C-8 of **6** and **7**, suggesting a similar structure. The strong ion observed at 153 ([M − $C_{14}H_{27}O$]$^+$) indicated a fragmentation at C-7−C-8 as seen for **6**. However, the ^{1}H NMR spectrum of **8** showed two triplets at δ 0.88 (H-18) and δ 2.55 (H-2′), a broad singlet at δ 1.25 (eight methylenes, H-9 to H-13 and H-15 to H-17), two overlapping multiplets at δ 1.60 (H-14) and δ 1.62 (H-1′), and an aldehyde proton at δ 9.77. The presence of two methylene signals at δ 2.55 and 1.62 next to an aldehyde group forming a CH_2CH_2CHO substructure was indicated by two coupled, isolated methylenes (COSY) correlated with an aldehyde group (HMBC). This was also consistent with the strong fragment ion observed at *m*/*z* 321 resulting from loss of CH_2CHO from the molecular ion, as shown in Figure 2.[26] The mass fragment ions at *m*/*z* 178 ([M − $COOCH_3$ − $C_8H_{15}O$] $^+$) and *m*/*z* 248 ([M − $COOCH_3$ − C_4H_9] $^+$) also indicated that the C_4H_9 and the C_3H_5O side chains were located at C-14 (δ 22.1 d). Finally, the assigned structure **8** was confirmed by HMBC correlations (C-14/H-1′, H-2′; C-14/H-15, H-16), as illustrated in Figure 2.

Plakortic acid (**9**) was isolated as a colorless oil, and its molecular formula was established as $C_{22}H_{38}O_4$ from its HREIMS spectrum. Its UV (221 nm) and IR showed the presence of an α,β-unsaturated carbonyl group (1690 cm^{-1}), an epoxy ring (1214 and 1099 cm^{-1}), and a carboxylic acid (1700 and 3502 cm^{-1}). The presence of unsaturated carbonyl and carboxylic acid groups was supported by the ^{13}C NMR values at δ 199.4 and δ 171.9, respectively. The presence of an acid group was further supported by the strong fragment at *m*/*z* 321 ([M − COOH]$^+$) in the mass spectrum. The ^{1}H NMR showed the presence of two olefinic protons at δ 6.46 and δ 6.49 (α,β-unsaturated carbonyl group), a singlet at δ 3.48, a doublet at δ 3.74 (epoxy ring), a triplet at δ 2.55 (J = 7.8 Hz), and a multiplet at δ 1.60 for two methylenes. The relationship of each proton and carbon was established from the COSY and HMBC spectra

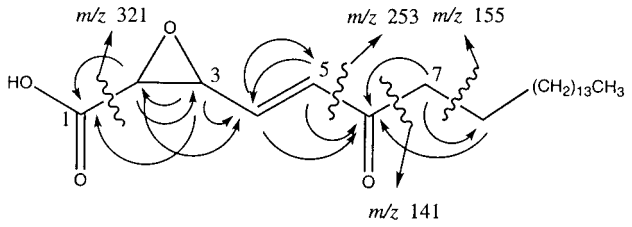


Figure 3. Selective HMBC and fragmentation of **9**.

Table 3. Cytotoxicities of Compounds **1**−**9** (IC_{50}, μg/mL)[a]

compound	KB-16	COLO-250
1	0.74	N[b]
2−**6**, **8**, **9**	N	N
7	3.43	0.28

[a] The concentration of compound that inhibited 50% (IC_{50}) of the growth of the human tumor cell lines, KB-16 (nasopharyngeal carcinoma) or COLO-250 (colon carcinoma) according to the method described previously.[27] [b] N: inactive.

of **9**. The fragment at *m*/*z* 141 in the mass spectrum formed by the breakage of the bond at C-6−C-7 clearly indicated the side chain as $C_{16}H_{33}$, which was supported by a multiplet at δ 1.60 for one methylene, a broad singlet at δ 1.25 for 13 methylene protons, and the end methyl protons observed as a triplet at δ 0.88 (J = 6.6 Hz) in its ^{1}H NMR. The isolated compounds were tested for cytotoxicity against human tumor cells in vitro. As shown in Table 3, compound **7** exhibited strong cytotoxicity against colon carcinoma (COLO-250) and weak activity against nasopharyngeal carcinoma (KB-16) cells with IC_{50} of 0.28 and 3.43 μg/mL, respectively, and compound **1** showed selective activity against human KB-16 cells at 0.74 μg/mL.

Experimental Section

General Experimental Procedures. Optical rotations were recorded on a JASCO DIP-1000 polarimeter. IR and UV spectra were measured on Hitachi T-2001 and Hitachi U-3210 spectrophotometers, respectively. EI and FABMS spectra were recorded on VG Quattro 5022 and JEOL JMS-HX 110 mass spectrophotometers. The ^{1}H, ^{13}C NMR, COSY, HMBC, and HSQC were recorded on Varian FT-300, Varian FT-400, and Bruker Avance 300 spectrometers. The chemical shifts are given in δ (ppm) and coupling constants in Hz. Si gel 60 (Merck) was used for column chromatography, and precoated Si gel plates (Merck, Kieselgel 60 F_{254}, 1 mm thickness) were used for preparative TLC.

Animal Material. The pale yellow sponge *Plakortis simplex* Schulze (SPST-3) was collected around Nan-wan, Taiwan, during June 1998, at a depth of 15 m and frozen shortly after collection. This sponge was identified by G. H. Lee, Institute of Oceanography, Academia Sinica. A voucher specimen (voucher No, SPST-3) was deposited in the Institute of Marine Resources, National Sun Yat-sen University.

Extraction and Isolation. The fresh sponge (330 g) was crushed in a blender with EtOH, and the material was extracted with the same solvent three times (1 L each time). The combined EtOH extract was concentrated, and the residue was diluted with water until the volume reached 500 mL. Then the suspension was extracted with EtOAc three times (500 mL each time). The EtOAc layer was concentrated to give a residue (6.45 gm), which was flash chromatographed with *n*-hexane/$CHCl_3$ and $CHCl_3$/MeOH mixtures to afford six fractions: A (0.24 g), B (0.32 g), C (0.11 g), D (3.21 g), E (0.41 g), and F (0.18 g). Fraction B on further chromatography (*n*-hexane/$CHCl_3$, 3:1) furnished plakorsin A (**6**, 8.7 mg). Fraction C on repeated chromatography (*n*-hexane/$CHCl_3$, 1:1) yielded dimethyl β-ketoadipate (**4**, 11 mg) and plakorsin C (**8**, 11 mg). Purification of fraction D (*n*-hexane/$CHCl_3$, 1:4) furnished chondrillin (**1**, 43.3 mg), 6-*epi*-chondrillin (**2**, 1.35 g), and 2-oxo-2,5-dihydrofuran-5-acetic acid methyl ester (**3**, 38 mg). Repeated chromatography over Si gel ($CHCl_3$/MeOH, 10:1) followed by the preparative TLC of fraction F furnished *cis*,*cis*-muconic acid methyl ester (**5**, 8 mg), plakorsin B (**7**, 13 mg), and plakortic acid (**9**, 8 mg).

Compound 4: colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.61 (t, J = 6.6 Hz, 2H), 2.86 (t, J = 6.6 Hz, 2H), 3.50 (s, 2H), 3.66 (s, OCH_3), 3.73 (s, OCH_3); EIMS (70 eV) *m*/*z* 188 (11), 156 (21), 129 (27), 125 (18), 115 (100), 101 (48), 97 (13), 84 (57), 59 (66).

Compound 5: white solid; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.09 (s, OCH_3), 6.23−6.47 (m, 2H), 8.25−8.60 (m, 2H), 12.4 (s, 1H); EIMS (70 eV) *m*/*z* 156 (4), 125 (14), 111 (51), 97 (100), 83 (12), 79 (16), 69 (22), 51 (18).

Plakorsin A (6): colorless oil; UV (MeOH) λ_{max} (log ϵ) 220 (3.13) and 281 (2.41) nm; IR ($CHCl_3$) ν_{max} 1739 (ester carbonyl), 1531, 1442, 1342, 1214, 1149, 1010, 964, and 775 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 2; EIMS (70 eV) *m*/*z* 364 (M^+, 27), 305 (11), 290 (2), 195 (7), 153 (77), 135 (8), 121 (17), 111 (41), 107 (32), 94 (58), 81 (29), 69 (28), 55 (80); HREIMS *m*/*z* 364.29707 $[M]^+$ (calcd for $C_{23}H_{40}O_3$, 364.29775).

Plakorsin B (7): amorphous solid; UV (MeOH) λ_{max} (log ϵ) 220.8 (2.93), 242.4 (1.39) and 283.2 (2.34) nm; IR ($CHCl_3$) λ_{max} 3579, 3039, 1704, 1519, 1446, 1346, 1218, 1010, 952, and 771 cm^{-1}; ^{1}H and ^{13}C NMR, see Tables 1 and 2; EIMS (70 eV) *m*/*z* 350 (M^+, 17), 305 (5), 290 (2), 195 (2), 181 (6), 153 (12), 139 (100), 121 (14), and 95 (39); HREIMS *m*/*z* 350.28082 $[M]^+$ (calcd for $C_{22}H_{38}O_3$, 350.28210).

Methylation of Plakorsin B (7). A solution of compound **7** (3 mg) in diethyl ether (2 mL) was treated with excess diazomethane and kept at 5 °C for 24 h. Usual workup of the reaction mixture furnished a product (2 mg) indistinguishable from compound **6** (R_f value, IR and ^{1}H NMR data).

Hydrolysis of Plakorsin A (6). To a solution of compound **6** (5 mg) in MeOH (3 mL) was added 0.5 M NaOH/MeOH (5 mL), and the reaction mixture was stirred for 30 min at room temperature. After acidification with 1 N HCl, the product (3 mg) was purified over a preparative TLC (Si gel) plate (1 mm thickness). The IR and ^{1}H NMR data of the hydrolyzed product were identical to those of **7**.

Plakorsin C (8): colorless oil; $[\alpha]^{25}_D$ + 25.8 (*c* 0.5, CH_2Cl_2); UV (MeOH) λ_{max} (log ϵ) 219 (2.93) and 282 (3.14) nm; IR ($CHCl_3$) ν_{max} 3016, 1735 (COOR), 1720 (CHO), 1523, 1446, 1365, 1214, 1145, 1018, and 771 cm^{-1}; ^{1}H and ^{13}C NMR, see Tables 1 and 2; EIMS (70 eV) *m*/*z* 364 (M^+, 36), 321 (4). 305 (24), 290 (4), 248 (2), 195 (9), 178 (5), 167 (13), 153 (100), 111 (46) and 95 (54); FABMS 387 $[M + Na]^+$; HREIMS *m*/*z* 364.29795 $[M]^+$ (calcd for $C_{22}H_{36}O_4$, 364.29775).

Plakortic acid (9): colorless oil; $[\alpha]^{25}_D$ + 36.3 (*c* 0.5, CH_2Cl_2); UV (MeOH) λ_{max} (log ϵ) 204 (1.89) and 221 (3.14); IR ($CHCl_3$) ν_{max} 3502 (OH), 1708 (COOH), 1690 (C=C−CO), 1457, 1388, 1292, 1214, 1099, 983, and 771 cm^{-1}; ^{1}H and ^{13}C NMR see Tables 1 and 2; EIMS (70 eV) *m*/*z* 366 (M^+, 3.6), 348 (5), 321 (5), 253 (9), 169 (9), 165 (6), 141 (6), 135 (7), 121 (13), 113 (7), 111 (14), 107 (26), 97 (42), 83 (30), 71(38), 57 (100); HREIMS *m*/*z* 366.27626 $[M]^+$ (calcd for $C_{22}H_{38}O_4$, 366.27701).

Acknowledgment. The authors thank Dr. G. H. Lee, Institute of Oceanology, Academia Sinica, for his identification of the sponge *Plakortis simplex*. We also acknowledge Ms. Chao-Lein Ho and Shiu-Ching Yu of NSC southern NMR and MS Instrument Center for measurement of NMR and MS spectral data. This investigation was supported by the National Science Council under grant NSC 89-2811-B-110-0002.

References and Notes

(1) Yoshioka, M.; Seikatsu Kagaku Kenyusho Kenkyu Hokoku (Miyagi Gaknin Joshi Daigaku) **1981**, *14*, 10−13; *Chem. Abstr.* **1982**, *96*, 65996w.
(2) Gunstone, F. D.; Wijesundera, R. C.; *J. Chem. Soc., Chem. Commun.* **1976**, 630−631, and references therein.
(3) Ishii, K.; Okajima, H.; Okada, Y.; Watanabe, H. *J. Biochem.* **1988**, *103*, 836−839.
(4) Ota, T. O.; Takagi, T. *Nippon Suisan Gakkaishi* (*Bull. Jpn. Soc. Sci. Fish.*) **1990**, *56*, 153−157.

(5) Ota, T. O.; Takagi, T. *Nippon Suisan Gakkaishi* (*Bull. Jpn. Soc. Sci. Fish.*) **1991**, *57*, 1565−1571.
(6) Ota, T. O.; Takagi, T. *Nippon Suisan Gakkaishi* (*Bull. Jpn. Soc. Sci. Fish.*) **1992**, *58*, 721−725.
(7) Batna, A.; Scheinkonig, J.; Spiteller, G. *Biochim. Biophys. Acta* **1993**, *1166*, 171−176.
(8) Okajima, H.; Ishii, K.; Watanabe, H. *Chem. Pharm. Bull.* **1984**, *32*, 3281−3286.
(9) Ishii, K.; Okajima, H.; Koyamatsu, T.; Okada, T.; Watanabe, H. *Lipids* **1988**, *23*, 694−700.
(10) Groweiss, A.; Kashman, Y. *Experientia* **1978**, *34*, 299.
(11) Ciminello, P.; Fattorusso, E.; Magno, S.; Magnoni, A.; Ialenti, A.; Di Rosa, M. *Experientia* **1991**, *47*, 739−743.
(12) Prinsep, M. R.; Blunt, J. W.; Munro, M. H. G. *J. Nat. Prod.* **1994**, *57*, 1557−1559.
(13) Hannemann, K.; Puchta, V.; Simon, E.; Ziegler, H.; Spiteller, G. *Lipids* **1989**, *24*, 296−298.
(14) Guth, H.; Grosch, W. *Fett. Wiss. Technol.* **1991**, *93*, 249−255.
(15) Guth, H.; Grosch, W. *Lebensm.-Unters. Forsch.* **1992**, *194*, 360−362.
(16) Scheinkonig, J.; Spiteller, G. *Leibigs Ann. Chem.* **1993**, 121−124.
(17) Shen, Y, C.; Tai, H. R.; Duh, C. Y. *Chin. J. Pharm.* **1996**, *48*, 1−10.
(18) Shen, Y. C.; Lin, S. L.; Duh, C. Y.; Huang, T. H. *J. Fish. Soc. Taiwan* **1995**, *22*, 365−374.
(19) Chen, C. Y.; Shen, Y. C.; Chen, Y. J.; Sheu, J. H.; Duh, C. Y. *J. Nat. Prod.* **1999**, *62*, 573−576.
(20) Quinoa, E.; Kho, E.; Manes, L. V.; Crews, P.; Bakus, G. J. *J. Org. Chem.* **1986**, *51*, 4260−4264.
(21) De Guzman, F. S.; Schmitz, F. J. *J. Nat. Prod.* **1990**, *53*, 926−931.
(22) Whitlock, B. J.; Whitlock, H. W. Jr. *J. Org. Chem.* **1974**, *39*, 3144.
(23) Tsuji, J.; Takayanagi, H. *J. Am. Chem. Soc.* **1974**, *96*, 7349−7350.
(24) Kubota, T. *Tetrahedron* **1958**, *4*, 68−86.
(25) Stierle, D. B.; Faulkner, D. J. *J. Org. Chem.* **1980**, *45*, 4980−4982.
(26) Silverstein, R. M.; Bassler, G. C.; Morrill, T. C. *Spectrometric Identification of Organic Compounds*, 5th ed.; John Wiley & Sons: New York, 1991; p 26.
(27) Kuo, Y. H.; Huang, H. C.; Kuo Yang, L. M.; Chen, C. F. *J. Org. Chem.* **1999**, *64*, 7023−7027.

NP000413D