cis-Clerodane Type Diterpenes from *Cistus monspeliensis*[1]

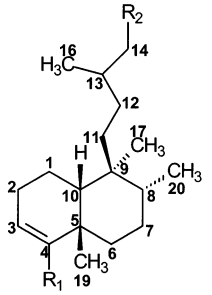
Eleftherios Kalpoutzakis, Nektarios Aligiannis, Alexios-Leandros Skaltsounis, and Sofia Mitakou*

Division of Pharmacognosy and Natural Product Chemistry, Department of Pharmacy, University of Athens, Panepistimiopolis Zografou, GR-15771, Athens Greece

Received September 11, 2002

The aerial parts of *Cistus monspeliensis* yielded 11 *cis*-clerodane type diterpenes. Five of these, **3**, **4**, **8**, **9**, and **10**, are new compounds. Their structures have been elucidated on the basis of their spectral data (FABMS, 1D and 2D NMR).

The genus *Cistus* comprises seven taxa in Greece. Among them, *Cistus monspeliensis* L. (Cistaceae) is a compact aromatic bush up to 1 m, erect and viscid. It is distinguished by its linear to linear-lanceolate, three-veined sticky aromatic, stalkless leaves and by its white, small, in rather one-side cluster flowers.[2,3] Although *C. monspeliensis* is one of the most common *Cistus* species in the Mediterranean area, there is only one phytochemical study where the presence of some clerodane type diterpenes was reported.[4] However in this 30-year-old publication, the relative stereochemistry of the asymmetric carbon atoms was not determined. As part of a research program toward the phytochemical study of the Cretan flora,[1] the aerial parts of *C. monspeliensis* were investigated. The present note reports the structural determination of five new *cis*-clerodane diterpenes (compounds **3**, **4**, **8**, **9**, and **10**). The establishment of the relative stereochemistry in C-5, C-8, C-9, and C-10 and the ^{1}H and ^{13}C NMR spectroscopic assignment of four clerodane diterpenes (compounds **1**, **2**, **5**, and **6**) previously isolated from this plant are also reported. Finally, the isolation of epi-populifolic acid[5] (**11**) for first time from this plant is also reported.



1 $R_1 = R_2 = CH_2OH$
2 $R_1 = CH_2OCOCH_3$, $R_2 = CH_2OH$
3 $R_1 = CH_2OCOCH_3$, $R_2 = CH_2OCOCH_3$
4 $R_1 = CH_2OH$, $R_2 = CH_2OCOCH_3$
5 $R_1 = CH_2OH$, $R_2 = CO_2H$
6 $R_1 = CO_2H$, $R_2 = CH_2OH$
7 $R_1 = CH_2OCOCH_3$, $R_2 = CO_2H$
8 $R_1 = CO_2H$, $R_2 = CH_2OCOCH_3$
9 $R_1 = CH{=}O$, $R_2 = CH_2OCOCH_3$
10 $R_1 = CH{=}O$, $R_2 = CH_2OH$
11 $R_1 = CH_3$, $R_2 = CO_2H$

A lipophilic extract of the aerial parts of *C. monspeliensis* was chromatographed on a silica gel column using a cyclohexane−CH_2Cl_2−MeOH gradient. Further chromatography of the main fractions yielded the new compounds **3**, **4**, **8**, **9**, and **10** as well as the previously reported 15,-18-dihydroxy-*cis*-clerodan-3-ene or cistadiol[4,6] (**1**), 15-hydroxy-18-acetoxy-*cis*-clerodane-3-ene[4] (**2**), 18-hydroxy-*cis*-clerodan-3-ene-15-oic acid[4] (**5**), 15-hydroxy-*cis*-clerodan-3-ene-18-oic acid[4] (**6**), 18-acetoxy-*cis*-clerodan-3-ene-15-oic acid[4,7] (**7**), and *cis*-clerodan-3-ene-15-oic acid or epi-populifolic acid[5] (**11**).

Compound **3** was obtained as a colorless gum. Its molecular formula was deduced to be $C_{24}H_{40}O_4$ on the basis of the pseudomolecular ion at *m/z* 391 [M − H]$^-$ in the HRFABMS. From the ^{1}H and ^{13}C NMR spectral data, which were assigned by COSY, HMQC, and DEPT 135 experiments (Tables 1 and 3, respectively) it was obvious that **3** corresponded to a clerodane type diterpene possessing two oxymethyl groups, two acetyl groups, one trisubstitued double bond, two tertiary methyl groups, and two secondary methyl groups. The NMR spectral data were similar to those of 15,18-diacetoxy-*trans*-clerodan-3-ene[8] with the exception of the chemical shift of C-19, which for compound **3** showed a 13.3 ppm downfield shift indicating that **3** should be the *cis*-isomer.[9−11] The AB ring *cis* fusion was also confirmed by NOESY data, where a clear cross-peak between H-19 (methyl group) (δ 1.06) and H-10 (δ 1.32) was observed. Moreover, the lack of NOE between the two methyl groups at C-9 (δ 0.72) and C-8 (δ 0.71) and H-10 indicated the *trans* relationships between the two methyl groups at C-9 and C-8 and H-10, respectively. Thus, compound **3** was identified as 15,18-diacetoxy-*cis*-clerodan-3-ene.

Compound **4** was obtained as a colorless gum. Its molecular formula was deduced to be $C_{22}H_{38}O_3$ on the basis of the pseudomolecular ion at *m/z* 349 [M − H]$^-$ in the HRFABMS. The ^{1}H and^{13}C NMR spectra (Tables 1 and 3, respectively) were similar to those of **3**, except that **4** had only one acetyl group. Moreover, the oxymethyl group at C-4 of **4**, in the ^{1}H NMR spectrum, appeared at higher field compared with those of **3**. These findings indicated that compound **4** should be the C-18 deacetylated derivative of **3**. The relative stereochemistry at C-5, C-8, C-9, and C-10 was confirmed, as for compound **3**, by NOESY experiments. Therefore, the structure of compound **4** was established as 15-acetoxy-18-hydroxy-*cis*-clerodan-3-ene.

Compound **8** was obtained as a colorless gum. Its molecular formula was deduced to be $C_{22}H_{36}O_4$ on the basis of the pseudomolecular ion at *m/z* 363 [M − H]$^-$ in the HRFABMS. The ^{1}H and^{13}C NMR spectra (Tables 2 and 3, respectively) indicated the presence of a *cis*-clerodan-3-ene system, an acetylated oxymethyl group, and a carboxylic group. The attachment of the carboxyl group at C-4 and

* To whom correspondence should be addressed. Tel: +3210-7274290. Fax: +3210-7274594. E-mail: mitakou@pharm.uoa.gr.

10.1021/np0204388 CCC: $25.00
Published on Web 01/23/2003

Table 1. ^{1}H NMR Data (δ) of Compounds **2**−**5** (400 MHz, $CDCl_3$)

position	2	3	4	5
1a	1.96 (1H, m)	1.98 (1H, m)	1.93 (1H, m)	1.96 (1H, m)
1b	1.78 (1H, dd, 14.8/8.7)	1.76 (1H, dd, 14.7/8.5)	1.77 (1H, dd, 14.5/8.5)	1.81 (1H, dd, 14.4/8.4)
2a	2.13[a]	2.20 (1H, m)	2.13[a]	2.19 (1H, m)
2b	2.11[a]	2.04[a]	2.11[a]	2.06 (1H, m)
3	5.65 (1H, brs)	5.64 (1H, brs)	5.58 (1H, brs)	5.59 (1H, brs)
6a	1.92 (1H, brd, 13.7)	1.92 (1H, brd, 13.4)	2.04 (1H, brd, 13.7)	2.01 (1H, brd, 13.6)
6b	1.13[a]	1.14[a]	1.13[a]	1.15[a]
7a	1.20[a]	1.23[a]	1.22[a]	1.26[a]
7b	1.20[a]	1.23[a]	1.22[a]	1.26[a]
8	1.39[a]	1.41[a]	1.38[a]	1.42[a]
10	1.34[a]	1.32 (1H, d, 6.2)	1.33 (1H, d, 6.4)	1.36[a]
11a	1.38[a]	1.38[a]	1.38[a]	1.39[a]
11b	1.15[a]	1.16[a]	1.19[a]	1.23[a]
12a	1.17[a]	1.12[a]	1.15[a]	1.21[a]
12b	1.00 (1H, m)	0.99 (1H, m)	1.00 (1H, m)	1.15[a]
13	1.43 (1H, m)	1.38[a]	1.40[a]	1.79 (1H, m)[a]
14a	1.62 (1H, m)	1.66 (1H, m)	1.64 (1H, m)	2.37 (1H, dd, 14.6/5.8)
14b	1.35[a]	1.39[a]	1.32[a]	2.11 (1H, dd, 14.6/8.2)
15	3.66 (2H, m)	4.07 (2H, m)	4.08[a]	
16	0.89 (3H, d, 6.4)	0.88 (3H, d, 6.3)	0.89 (3H, d, 6.4)	0.97 (3H, d, 6.4)
17	0.73 (3H, s)	0.72 (3H, s)	0.72 (3H, s)	0.73 (3H, s)
18a	4.58 (1H, d, 14.0)	4.57 (1H, d, 13.7)	4.20 (1H, d, 13.5)	4.20 (1H, d, 13.2)
18b	4.53 (1H, d, 14.0)	4.52 (1H, d, 13.7)	4.08[a]	4.08 (1H, d, 13.2)
19	1.07 (3H, s)	1.06 (3H, s)	1.07 (3H, s)	1.08 (3H, s)
20	0.72 (3H, d, 6.4)	0.71 (3H, d, 6.4)	0.70 (3H, d, 6.4)	0.71 (3H, d, 6.4)
CH_3CO	2.04 (3H, s)	2.03 (3H, s)	2.04 (3H, s)	
CH_3CO		2.01 (3H, s)		

[a] Assignment determined by HMQC and COSY experiments. Multiplicity not determined (signal overlap).

Table 2. ^{1}H NMR Data (δ) of Compounds **6** and **8**−**10** (400 MHz, $CDCl_3$)

position	6	8	9	10
1a	1.95 (1H, m)	1.97 (1H, m)	1.95 (1H, m)	1.94 (1H, m)
1b	1.82 (1H, dd, 14.5/8.7)	1.80 (1H, dd, 14.8/8.8)	1.83 (1H, dd, 15.0/9.0)	1.84 (1H, dd, 15.0/9.0)
2a	2.32 (1H, m)	2.32 (1H, m)	2.52 (1H, m)	2.52 (1H, m)
2b	2.18 (1H, m)	2.20 (1H, m)	2.36 (1H, m)	2.36 (1H, m)
3	6.76 (1H, brt, 3.6)	6.78 (1H, brt, 3.7)	6.68 (1H, brt, 3.7)	6.69 (1H, brt, 3.5)
6a	2.66 (1H, dd, 12.7/4.1)	2.68 (1H, dd, 12.7/4.1)	3.07 (1H, dd, 11.9/4.3)	3.07 (1H, dd, 12.4/4.6)
6b	1.09[a]	1.09[a]	1.08[a]	1.07[a]
7a	1.25[a]	1.22[a]	1.23[a]	1.23[a]
7b	1.25[a]	1.22[a]	1.23[a]	1.23[a]
8	1.40[a]	1.43[a]	1.43[a]	1.45[a]
10	1.40[a]	1.40[a]	1.39[a]	1.35 [a]
11a	1.42[a]	1.41[a]	1.38[a]	1.42[a]
11b	1.21[a]	1.19[a]	1.19[a]	1.21[a]
12a	1.20[a]	1.20[a]	1.18[a]	1.23[a]
12b	1.07[a]	1.07[a]	1.03 (1H, m)	1.07[a]
13	1.38[a]	1.42[a]	1.39[a]	1.44[a]
14a	1.63 (1H, m)	1.67 (1H, m)	1.67 (1H, m)	1.62 (1H, m)
14b	1.40[a]	1.40[a]	1.38[a]	1.40[a]
15	3.67 (2H, m)	4.08 (2H, m)	4.09 (2H, m)	3.67 (2H, m)
16	0.89 (3H, d, 6.2)	0.90 (3H, d, 6.2)	0.89 (3H, d, 6.4)	0.89 (3H, d, 6.4)
17	0.73 (3H, s)	0.74 (3H, s)	0.67 (3H, s)	0.67 (3H, s)
18a			9.38 (1H, s)	9.38 (1H, s)
18b				
19	1.19 (3H, s)	1.20 (3H, s)	1.09 (3H, s)	1.10 (3H, s)
20	0.71 (3H, d, 6.6)	0.72 (3H, d, 6.6)	0.71 (3H, d, 6.4)	0.70 (3H, d, 6.5)
CH_3CO		2.03 (3H, s)	2.04 (3H, s)	
CH_3CO				

[a] Assignment determined by HMQC and COSY experiments. Multiplicity not determined (signal overlap).

the acetoxymethyl group at C-14 was deduced from the HMBC spectrum, where the $^3J_{CH}$ strong cross-peak between the C-18 carboxyl group (δ 173.2) and H-3 (δ 6.78) and the $^2J_{CH}$ cross-peak between the C-15 oxymethyl group (δ 63.1) and H-13 (δ 1.42) signals were observed. Therefore, compound **8** was 5-acetoxy-*cis*-clerodan-3-ene-18-oic acid.

Compounds **9** and **10** were both obtained as gums. Their molecular formulas were determined by HRFABMS as $C_{22}H_{36}O_3$ and $C_{20}H_{34}O_2$, respectively. The ^{1}H and ^{13}C NMR spectra (Tables 2 and 3, respectively) were similar to those of compounds **8** and **6**, respectively, except that in **9** and **10** the C-4 carboxyl group was replaced by an aldehydic function. For both compounds, the C-4 aldehyde group (δ 194.2 and 194.4) was deduced from its long-range C−H correlation with the H-3 olefinic proton (δ 6.68 and 6.69, respectively) in the HMBC spectra. Therefore, the structures were established to be 15-acetoxy-*cis*-clerodan-3-ene-18-al (**9**) and 15-hydroxy-*cis*-clerodan-3-ene-18-al (**10**), respectively. It is noteworthy that there are few examples[9,12−14] of a clerodan-3-ene with an aldehydic function at C-4, due to the high instability of these compounds and their rapid oxidation to the corresponding carboxylic analogues.

Experimental Section

General Experimental Procedures. Optical rotations were measured on a Perkin-Elmer 341 polarimeter. ^{1}H NMR (400 MHz) and ^{13}C NMR (50 MHz) data were recorded on a Bruker DRX400 spectrometer and a Bruker AC200 spectrometer, respectively (using TMS as an internal standard). COSY,

Table 3. ^{13}C NMR Data (δ) of Compounds **1**−**6** and **8**−**11** (50 MHz, $CDCl_3$)

position	**1**	**2**	**3**	**4**	**5**	**6**	**8**	**9**	**10**	**11**
1	17.3	17.2	17.2	17.3	17.3	16.8	16.8	16.8	16.9	17.6
2	23.7	23.9	23.9	23.7	23.7	24.4	24.4	25.8	25.8	24.7
3	124.6	129.2	129.2	124.8	125.0	142.1	142.3	155.9	156.1	123.1
4	143.2	138.3	138.3	143.2	143.1	137.8	137.7	147.5	147.7	139.9
5	36.1	36.2	36.2	36.2	36.2	36.3	36.3	36.6	36.8	36.8
6	36.7	37.2	37.2	36.8	36.8	36.8	36.8	35.5	35.4	37.7
7	28.9	28.7	28.7	28.9	28.9	28.7	28.7	28.5	28.5	28.7
8	37.2	37.2	37.2	37.2	37.3	37.7	37.6	37.3	37.5	37.2
9	39.9	39.8	39.9	39.9	40.1	40.1	40.1	40.0	40.0	41.5
10	45.0	44.9	44.9	45.0	45.1	45.3	45.2	44.9	45.6	44.5
11	35.0	35.0	35.0	35.4	35.0	35.2	35.1	35.2	35.0	35.0
12	29.6	29.6	29.4	29.4	29.2	29.7	29.5	29.5	29.5	29.6
13	30.1	30.1	30.6	30.5	30.9	30.2	30.5	30.5	30.5	30.9
14	39.7	39.8	35.0	35.4	41.4	39.9	35.4	35.4	39.5	41.4
15	61.0	61.2	63.1	63.1	178.9	61.2	63.1	63.1	60.9	179.0
16	19.8	19.8	19.6	19.6	19.9	19.8	19.6	19.6	19.9	19.7
17	17.4	17.4	17.4	17.4	17.4	18.2	18.2	18.1	18.0	17.3
18	64.5	66.6	66.6	64.8	64.7	173.1	173.2	194.2	194.4	19.9
19	34.9	34.6	34.6	35.0	35.0	33.3	33.3	33.1	33.1	33.0
20	15.8	15.9	15.9	15.9	15.8	15.9	15.8	15.9	15.9	15.9
CH_3CO		21.2	21.2 21.0	21.0			21.0	21.0		
CH_3CO		170.9	173.2 170.9	171.2			171.3	171.0		

HMQC, HMBC, and NOESY (mixing time 950 ms) NMR data were obtained using standard Bruker microprograms. FABMS and HRFABMS were recorded using ZAB HF and AEI MS-902 spectrometers, in a glycerol matrix in negative-ion mode. Column chromatography was carried out using silica gel 60 (Merck, 0.015−0.040 mm) with an applied pressure of 300 mbar. TLC was carried out on glass precoated silica gel 60 F_{254} plates (Merck).

Plant Material. The aerial parts of *Cistus monspeliensis* collected in June 1999, near the villages Sisi and Milato in E. Crete, Greece, were identified by one of us (E.K.). A voucher specimen has been deposited at the Herbarium of the University of Athens, Departement of Pharmacognosy (KL060).

Extraction and Isolation. Air-dried, powdered plant material (2.3 kg) was extracted with CH_2Cl_2 (6 L × 3) and then MeOH (6 L × 3). The CH_2Cl_2-soluble extract was concentrated under reduced pressure to give a residue (210 g). A part of this extract (42 g) was chromatographed over a silica gel 60H column and eluted with cyclohexane−CH_2CI_2 (100:0 → 0:100) and CH_2Cl_2−MeOH (100:0 → 0:100) (0.5−3.5 L) to give 24 fractions. The seventh of these fractions (0.56 g), eluted with CH_2Cl_2, was rechromatographed over a flash silica gel column using a cyclohexane−AcOEt gradient (97:3 → 85:15) to afford compounds **3** (95 mg), **9** (20 mg), and **8** (22 mg). Fraction 8 (1.3 g), eluted with CH_2Cl_2, was chromatographed over a flash silica gel column and eluted with cyclohexane−AcOEt (98:2 → 50:50) to give compounds **11** (24 mg), **2** (18 mg), and **4** (25 mg). Fraction 11 (1.4 g), eluted with CH_2Cl_2−MeOH (98:2), was chromatographed over a flash silica gel column and eluted with a cyclohexane−AcOEt gradient (95:5 → 85:15) to give compounds **10** (25 mg) and **7** (164 mg). Finally, the 13th fraction (1.05 g), eluted with CH_2Cl_2−MeOH (97:3), was rechromatographed over silica gel and eluted with CH_2Cl_2−MeOH (99.5:0.5 → 98:2) to afford compounds **1** (123 mg), **5** (22 mg), and **6** (18 mg).

All compounds were identified by means of spectral data (^1H NMR, ^{13}C NMR, DEPT 135, and HRFABMS). The relative stereochemistry of these compounds and the complete assignment of protons and carbons were established using 2D ^1H−^1H COSY, 2D ^1H−^1H NOESY, HMQC, and HMBC NMR spectroscopy.

15,18-Dihydroxy-*cis*-clerodan-3-ene, or Cistadiol (1): colorless gum; $[\alpha]^{20}_D$ +34° (*c* 0.9, $CHCl_3$); HRFABMS *m/z* [M − H]$^-$ 307.2719 (calcd 349.2715 for $C_{20}H_{35}O_2$).

18-Acetoxy-3-ene-*cis*-clerodan-15-ol (2): colorless gum; $[\alpha]^{20}_D$ +24° (*c* 0.6, $CHCl_3$); ^1H NMR data, see Table 1; ^{13}C NMR data, see Table 3; HRFABMS *m/z* [M − H]$^-$ 349.2818 (calcd 349.2821 for $C_{22}H_{37}O_3$).

15,18-Diacetoxy-3-ene-*cis*-clerodane (3): colorless gum; $[\alpha]^{20}_D$ +32° (*c* 0.4, $CHCl_3$); ^1H NMR data, see Table 1; ^{13}C NMR data, see Table 3; HRFABMS *m/z* [M − H]$^-$ 391.2923 (calcd 391.2926 for $C_{24}H_{39}O_4$).

15-Acetoxy-3-ene-*cis*-clerodan-18-ol (4): colorless gum; $[\alpha]^{20}_D$ +37° (*c* 0.4, $CHCl_3$); ^1H NMR data, see Table 1; ^{13}C NMR data, see Table 3; HRFABMS *m/z* [M − H]$^-$ 349.2819 (calcd 349.2821 for $C_{22}H_{37}O_3$).

18-Hydroxy-*cis*-clerodan-3-ene-15-oic acid (5): colorless gum; $[\alpha]^{20}_D$ +11° (*c* 0.3, $CHCl_3$); ^1H NMR data, see Table 1; ^{13}C NMR data, see Table 3; HRFABMS *m/z* [M − H]$^-$ 321.2505 (calcd 321.2508 for $C_{20}H_{33}O_3$).

15-Hydroxy-*cis*-clerodan-3-ene-18-oic acid (6): colorless gum; $[\alpha]^{20}_D$ +41° (*c* 0.2, $CHCl_3$); ^1H NMR data, see Table 2; ^{13}C NMR data, see Table 3; HRFABMS *m/z* [M − H]$^-$ 321.2506 (calcd 321.2508 for $C_{20}H_{33}O_3$).

18-Acetoxy-*cis*-clerodan-3-ene-15-oic acid (7): colorless gum; $[\alpha]^{20}_D$ +18° (*c* 0.7, $CHCl_3$); HRFABMS *m/z* [M − H]$^-$ 363.2610 (calcd 363.2613 for $C_{22}H_{35}O_4$).

15-Acetoxy-*cis*-clerodan-3-ene-18-oic acid (8): colorless gum; $[\alpha]^{20}_D$ +41° (*c* 0.4, $CHCl_3$); ^1H NMR data, see Table 2; ^{13}C NMR data, see Table 3; HRFABMS *m/z* [M − H]$^-$ 363.2611 (calcd 363.2613 for $C_{22}H_{35}O_4$).

15-Acetoxy-*cis*-clerodan-3-ene-18-al (9): colorless gum; $[\alpha]^{20}_D$ +7° (*c* 0.2, $CHCl_3$); ^1H NMR data, see Table 2; ^{13}C NMR data, see Table 3; HRFABMS *m/z* [M − H]$^-$ 347.2662, calcd 347.2664 for $C_{22}H_{35}O_3$.

15-Hydroxy-*cis*-clerodan-3-ene-18-al (10): colorless gum; $[\alpha]^{20}_D$ +20° (*c* 0.2, $CHCl_3$); ^1H NMR data, see Table 2; ^{13}C NMR data, see Table 3; HRFABMS *m/z* [M − H]$^-$ 305.2557 (calcd 305.2559 for $C_{20}H_{33}O_2$).

***cis*-Clerodan-3-ene-15-oic acid or epi-populifolic acid (11):** colorless gum; $[\alpha]^{20}_D$ +11° (*c* 0.3, $CHCl_3$); HRFABMS *m/z* [M − H]$^-$ 305.2556 (calcd 305.2559 for $C_{20}H_{33}O_2$).

References and Notes

(1) Part 7 in the series Cretan Plants. For Part 6, see: Melliou, E.; Magiatis, P.; Skaltsounis, A. L. *J. Agric. Food Chem.*, in Press.
(2) Warburg, E. F. *Flora Europea*; Cambridge University Press, Vol. 2, 1968; p 283
(3) Polunin, O. *Flowers of Greece and the Balkans*; Oxford University Press, 1987; p 340.
(4) Tabacik, C.; Bard, M. *Phytochemistry* **1971**, *10*, 3093−3109.
(5) Leitao, G., Kaplan, C., Galeffi, C. *Phytochemistry* **1992**, *31*, 3277−3279.
(6) Berti, G.; Livi, O.; Segnini, D. *Tetrahedron Lett.* **1970**, *17*, 1401−1404.
(7) Kolocouris, A.; Mavromoustakos, T.; Demetzos, C.; Terzis, A.; Grdaldonik, S. G. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 837−840.
(8) San-Martin, A.; Rovirosa, J.; Labbe, C., Givovich, A.; Mahu, M.; Castillo, M. *Phytochemistry* **1986**, *25*, 1393−1395.

(9) Zdero, C.; Bohlmann, F.; King, M. *Phytochemistry* **1991**, *30*, 2991−3000.
(10) Heymann, H.; Tezuka, Y.; Kikuchi, T.; Supriyatna, S. *Chem. Pharm Bull.* **1994**, *42*, 1202−1207.
(11) Kuroyanagi, M.; Ushida, K.; Ueno, A.; Satake, M.; Shimomura, K. *Phytochemistry* **1993**, *34*, 1377−1384.
(12) Jamora, C.; Theodoraki, M.; Malhotra, V.; Theodorakis, E. *Bioorg. Med. Chem.* **2001**, *9*, 1365−1370.
(13) Lajide, L.; Escoubas, P.; Mizutani, J. *Phytochemistry* **1995**, *40*, 1101−1104.
(14) Bohlmann, F.; Zdero, C.; Gupta, R.; King, R.; Robinson, H. *Phytochemistry* **1980**, *19*, 2695−2705.

NP0204388