Journal of Natural Products
Vol. 58, No. 8, pp. 1185-1191, August 1995

THE STRUCTURE OF A NOVEL CEMBRANOID DITERPENE FROM A PHILIPPINE COLLECTION OF THE SOFT CORAL *SINULARIA FLEXIBILIS*

P.P. GUERRERO, R.W. READ,*

School of Chemistry, University of New South Wales, Sydney, New South Wales 2052, Australia

M. BATLEY,*

School of Chemistry, Macquarie University, North Ryde, New South Wales 2109, Australia

and G.C. JANAIRO

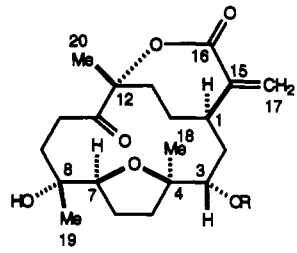
Department of Chemistry, De La Salle University, 2401 Taft Avenue, Manila, Philippines

ABSTRACT.-A new optically active diterpene lactone, sinulariolone [**1**], has been isolated as the major secondary metabolite in a Philippine collection of *Sinularia flexibilis*. The compound has a tricyclic structure and is more highly oxygenated than previously reported diterpenes from this species. The structure of **1** was elucidated by spectroscopy and its relative stereochemistry confirmed by single-crystal X-ray crystallography.

At least 12 cembranoid diterpenes have been isolated from the alcyonacean soft coral *Sinularia flexibilis* Quoy and Gaimard (family Alcyoniidae, order Alcyonaceae) (1–6). Most are derivatives of sinulariolide (1,7) or flexibilide (5,8) [sinularin (3)], which contain a 14-membered carbocycle fused to a 6- or 5-membered lactone ring, respectively. Recently, a new cladiellane diterpene (9) and three new lobane diterpenes (10) were isolated from an Okinawan collection. Significant differences occur in the relative amounts of diterpenes found in specimens of *S. flexibilis* collected from reefs in Indonesia (1), Australia (3,5), the Red Sea (4), and Japan (6,9,10). In addition, various ratios of the cembranoid compounds have been noted within collections from different parts of the Great Barrier Reef, Australia (5), and in a separate study these variations have been linked to environmental factors (11). This variability of constituents prompted us to study a Philippine collection of the octocoral *S. flexibilis*. We report herein the isolation of a new cembranoid diterpene, sinulariolone [**1**], that is more highly oxygenated than those reported previously.

RESULTS AND DISCUSSION

The CH_2Cl_2-soluble portion of the EtOH extracts of *S. flexibilis* collected from Galvez Reef in the Philippines yielded, after chromatography, two sterol-containing fractions, along with fractions containing an unknown cembranoid, and two fractions containing trace amounts of unidentified metabolites. A hydrate of the novel cembranoid crystallized from Et_2O as colorless prisms, mp 215–216°, $[\alpha]^{25}D$ −15.8°. The molecular formula $C_{20}H_{30}O_6 \cdot H_2O$ was established by elemental analysis, while the highest mass peak in the mass spectrum at *m/z* 349 corresponded to loss of a hydroxyl group from the absent parent ion (*m/z* 366). The ir spectrum contained carbonyl absorptions at ν max 1720, 1700, and 1620 cm^{-1}, consistent with the presence of ketone and α,β-unsaturated ester functions and a hydroxyl functionality (ν max 3400–3200 cm^{-1}). The presence in the ^1H-nmr spectrum of two doublet resonances at δ 6.19 and 5.52, the latter with allylic coupling, suggested that the ester was part of an exo-methylene lactone ring. This was supported by ^{13}C-nmr resonances at δ 124.0 (t), 146.5 (s), and 168.4 (s) (see Table 1). There was also one very low-field ^{13}C-nmr signal (δ 211.0) corresponding to a ketone. In addition, signals were observed at δ 73.7 (s), 74.5 (d), 85.4 (d), 88.0 (s), and 91.5 (s) which were assigned to carbons singly bound to oxygen; no signals occurred in the region



1 R=H
2 R=Ac

expected for epoxide carbons, typically δ 55–65 (12–14). The quaternary carbon signal at δ 91.5 coincided almost exactly with the signal reported for the lactone carbon, C-12, in sinulariolide (1), although there was less similarity between the carbinol signals and the lactone resonance of flexibilide [δ ($CDCl_3$) 82.6 (d); δ [$(CD_3)_2SO$] 81.8 (d)] (8). These features prompted the tentative assignment of structure **1** as a sinulariolide derivative, named sinulariolone, with numbering as shown in **1**.

TABLE 1. Selected Nmr Spectroscopic Data for Sinulariolone [**1**] and Sinulariolone Acetate [**2**].[a]

Position	**1**[c]		**2**[d]
	δ_C [No. H]	δ_H [mult., *J* (Hz)]	δ_H [mult., *J* (Hz)]
1	33.1 (1)	3.16 (ddddd, 11.8, 11.4, 6.4, 1.9, 1.4)	3.06 (m)
2	37.9 (2)	1.69 (ddd, 13.4, 11.8, 3.2)	1.62 (ddd, 13.2, 12.0, 2.7)
		1.89 (ddd, 13.4, 11.5, 1.9)	1.94 (m)
3	74.5 (1)	3.58 (dd, 11.5, 3.2)	4.74 (dd, 11.4, 2.7)
4	88.0 (0)		
5	39.0 (2)	1.67 (ddd, 12.2, 10.6, 9.0, 0.2)	1.54 (ddd, 12.5, 10.3, 7.9)
		1.79 (ddd, 12.2, 7.5, 4.6)	1.72 (ddd, 12.5, 8.8, 4.2)
6	25.8 (2)	1.91 (m)	1.90 (m)
		1.95 (m)	1.95 (m)
7	85.4 (1)	4.01 (dd, 7.9, 6.6)	4.00 (dd, 7.4, 7.2)
8	73.7 (0)		
9	35.5 (2)	1.76 (dddd, 14.0, 8.1, 2.9, 0.6)	1.67 (ddd, 13.1, 5.0, 2.6)
		2.13 (ddd, 14.0, 10.4, 2.7)	2.22 (m)
10	34.5 (2)	2.63 (ddd, 20.9, 8.1, 2.7)	2.63 (ddd, 20.8, 8.1, 3.7)
		3.62 (ddd, 20.9, 10.4, 2.9)	3.61 (ddd, 20.8, 9.3, 3.7)
11	211.0 (0)		
12	91.5 (0)		
13	34.8 (2)	1.93 (ddd, 15.3, 12.7, 6.2)	not defined
		2.35 (ddd, 15.3, 6.2, 1.5)	2.39 (ddd, 15.2, 6.0, 1.2)
14	31.3 (2)	1.13 (dddd, 12.9, 11.4, 6.2, 1.5)	not defined
		2.15 (dddd, 12.9, 12.7, 6.4, 6.2)	2.19 (dddd, 12.8, 12.8, 6.4, 6.4)
15	146.5 (0)		
16	168.4 (0)		
17	124.0 (2)	5.52 (t, 1.2)	5.42 (dd, 1.1, 0.8)
		6.19 (d, 1.1)	6.32 (d, 0.7)
18	16.9 (3)	1.05 (d, 0.2)	1.15 (s)
19	22.7 (3)	1.09 (d, 0.6)	1.16 (s)
20	29.6 (3)	1.40 (s)	1.47 (s)

[a]Chemical shifts are reported as ppm from internal TMS.
[b]Numbering according to structures **1** and **2**.
[c]Recorded in $(CD_3)_2CO$; signal at δ 29.76 used as a secondary standard for the ^{13}C-nmr spectra.
[d]Recorded in $CDCl_3$.

The non-methyl proton signals fell into three nmr spin-systems. With the H-17 and H-17′ resonances unambiguously assigned on the basis of their chemical shifts, the phase-sensitive double-quantum filtered COSY spectrum was used to make assignments for all the protons from H-1 to H-3 and for H-13α, -13β and H-14α, -14β (α and β refer to faces of the molecule as drawn in structure **1**) on the basis of observed *J* connectivities. Coupling was also seen between H-9α, -9β and H-10α, -10β and both H-7 and H-5α, -5β were coupled to a signal or signals in the congested region near δ 1.9. The TOCSY pulse sequence (15) and used to prove that H-7 and H-5α, -5β belonged to the same spin-system and that the H-6α, -6β resonances were near δ 1.9. Small splittings of about 0.5 Hz were observed on the methyl resonances at δ 1.05 and 1.09 and homonuclear difference decoupling was used to demonstrate that the couplings were to H-5α and H-9α, respectively. Finally, the ^{1}H-^{1}H coupling constants were measured from the one-dimensional proton spectrum, using the phase-sensitive COSY spectrum and, on occasion, difference decoupling to assign the splittings within each multiplet. These are recorded in Table 1; only the value for $J_{6\alpha,6\beta}$ remained poorly defined.

As mentioned earlier, the ^{13}C-nmr resonances of C-15, C-16, and C-17 were identifiable from their chemical shifts. All other protonated carbons were assigned from the ^{1}H-^{13}C chemical shift correlation spectrum and the number of protons attached to each carbon was confirmed using the DEPT pulse sequence (16). The quaternary carbons could not be assigned by two-dimensional correlation spectra via long-range coupling in the direct mode, because the amount of sample was insufficient, but similar information was obtained by selective proton excitation with polarization transfer via long-range coupling (17). In this way, all the ^{13}C-nmr resonances were assigned and the connections between the separate proton spin-systems established, including location of the keto group at C-11.

Acetylation of the substance afforded a monoacetate **2** [δ 2.04 (s)] with a one-proton signal at δ 4.74 (dd) in place of the multiplet at δ 3.56 corresponding to H-3 in the natural product (Table 1). Compound **1** clearly had one secondary hydroxyl group. The remaining degree of unsaturation and two non-carbonyl oxygens were best accommodated as one tertiary hydroxyl group and one cyclic ether. Because epoxide rings had been excluded, the ether linkage was placed between C-4 and C-7, leaving the remaining tertiary alcohol at C-8. The relatively high chemical shifts at C-4 and C-7 were then also consistent with those for corresponding carbons in the tetrahydrofuran portions of an unnamed 8,11-ether bridged sinularolide from Okinawan *S. flexibilis* (δ 85.4, C-8; 83.4, C-11) (6) and pachyclavularolide (δ 84.8, C-9; 84.0, C-12) (18). The compound was therefore confirmed to be a hydrate and the molecule deduced to have structure **1**, excluding stereochemistry.

Cross-peak intensities in the phase-sensitive NOESY spectrum (19) of **1** obtained with a mixing time of 1 sec were between −0.1 and −0.2 of the intensities of the diagonal peaks (Table 2), that is, close to the theoretical maximum in the fast motional limit. Cross-peaks between more widely separated protons were in the range of −0.02 to −0.008. Combination of the nOe information with the proton-proton coupling constants, together with the assumption that the configuration around C-1 was *R* [corresponding to (*R*)-cembrene], permitted assignment of the stereochemical orientation of the remaining five stereogenic centers. The assignment of C-3 was based on $J_{1,2\beta}$, $J_{2\alpha,3}$ and the H-1/H-2α, H-2β/H-17 and H-2α/H-17 NOESY peaks (Table 2); C-4 on the H-1/H-18 and H-2α/H-18 NOESY peaks and the coupling constants between H-5α, H-5β, H-6α, and H-6β; C-7 on H-7/H-9α and H-7/H-18 NOESY peaks; C-8 on the H-6β/H-19 and H-7/H-9α NOESY peaks, absence of H-7/H-19 correlations, and the four H-9 and H-10 coupling constants; and the C-12 assignment was based on the

TABLE 2. NOESY Spectroscopic Data for Sinulariolone [**1**].[a]

Proton[b]	δ (ppm)	Protons that gave nOe (NOESY peak area)
1	3.16	H-2α (2), H-10β (8), H-18 (1.5)
2α	1.89	H-1, H-2β, H-17 (3), H-18 (5)
2β	1.69	H-2α (9), H-3 (6), H-17 (3)
3	3.58	H-2β
5α	1.67	H-5β (7), H-6β (1.5)
5β	1.79	H-5α
6β	1.95	H-5α, H-7 (3), H-9α (2), H-19 (3)
7	4.01	H-6β, H-9α (3), H-18 (3)
9α	1.76	H-6β, H-7, H-9β (11), H-10α (3)
9β	2.13	H-9α
10α	2.63	H-9α, H-10β (18); H-20 (1.5)
10β	3.62	H-1, H-10α
13α	2.35	H-13β, H-14α (5), H-20 (3)
13β	1.93	H-13α (13)
14α	2.15	H-13α, H-14β
14β	1.13	H-14α (14)
17	5.52	H-2α, H-2β, H-17′ (16)
17′	6.19	H-17
18	1.05	H-1, H-2α, H-7
19	1.09	H-6β
20	1.40	H-13α

[a]Chemical shifts are reported as ppm from internal TMS. Recorded in $(CD_3)_2CO$.
[b]Numbering according to structures **1** and **2**; α and β refer to faces of the molecule.

H-13α/H-20 NOESY peaks. Few attempts have been made to determine the solution structures of cembranoids (18).

Single-crystal X-ray crystallographic analysis confirmed the solid-state molecular structure as shown in Figure 1 (also see Table 3) and the presence in sinulariolone [**1**] of the ether bridge. It also supported the spectroscopic assignment of relative configuration at the six stereogenic centers and clarified the position of the solvent H_2O molecule as most closely associated with the tertiary hydroxyl group at C-8. The structure is clearly related to sinulariolide and other seven-membered lactonic cembrane diterpenes isolated from *S. flexibilis* and less closely to flexibilide derivatives. The stereochemical configurations at C-1, C-4, and C-12 are identical to those in sinulariolide. Conversion of sinulariolide into **1** should be possible by simple oxidation and epoxide opening steps.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—The mp is uncorrected and was determined on a Buchi 510 oil immersion apparatus. Microanalysis was performed by Dr. H.P. Pham of the Microanalytical Unit, School of Chemistry, University of New South Wales. Mass spectra were measured on a Kratos MS25 or on a VG Quattro mass spectrometer in eims (70 eV, source temperature 180° or 220°) and cims (NH_3, source temperature 220°) modes. The optical rotation measurement was made on an AA-10 automatic polarimeter. The ir spectrum was recorded on a Bio-Rad FTS-7 Ft-ir spectrophotometer and the uv spectrum on a Carey 1 recording spectrophotometer. The ^1H- and ^{13}C-nmr spectra were recorded on a Varian XL-400 spectrometer at 20°; chemical shifts were measured relative to internal TMS (^1H) or to the $(CD_3)_2CO$ solvent peak at δ 29.76. Merck type 60 Si gel was used for vlc (20) and pre-coated plates of Merck Si gel 60G F_{254} on aluminum sheets were used for tlc.

ANIMAL MATERIAL.—Samples of *Sinularia flexibilis* were collected at a depth of approximately 5 meters at high tide from the Galvez Reef in Talim Bay, Matuod, Lian Batangas, Philippines, in November 1989. A voucher specimen (No. G15604) has been deposited with the Australian Museum, Sydney.

EXTRACTION AND ISOLATION.—Fresh coral (800 g) was macerated in a blender and repeatedly extracted

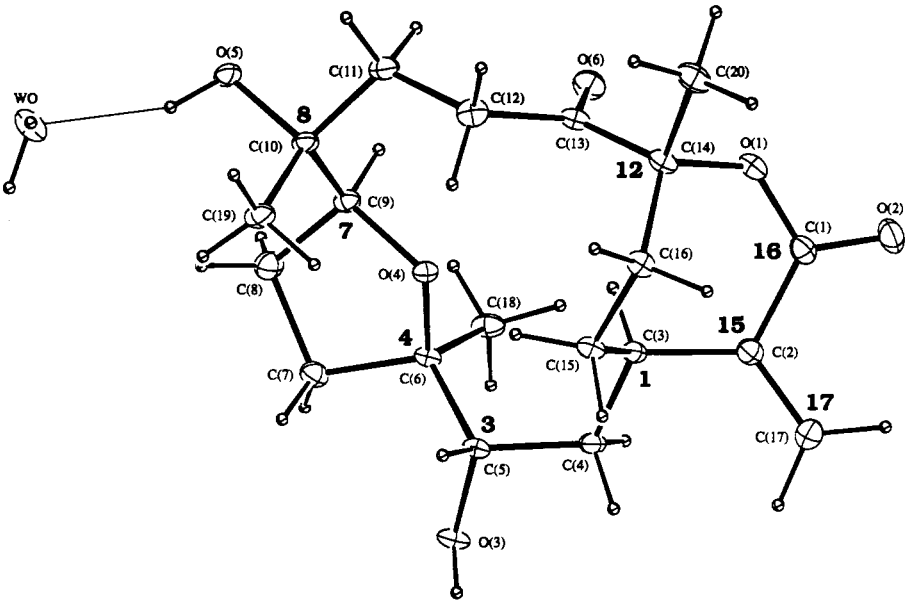


FIGURE 1. ORTEP drawing from the X-ray crystal structure of sinulariolone [**1**] (numbers in bold refer to systemic numbering).

TABLE 3. Non-Hydrogen Atomic Parameters for **1** (Esd in parentheses).

Atom[a]	*x*	*y*	*z*	B_{eq} (Å^2)[b]
O-1	0.7460	0.4863	0.6864	4.63 (5)
O-2	0.4967 (4)	0.6608 (3)	0.7611 (3)	5.98 (7)
O-3	0.8728 (4)	1.0854 (3)	0.1044 (2)	4.06 (4)
O-4	0.9542 (3)	0.6349 (2)	0.2256 (2)	3.28 (3)
O-5	1.1589 (4)	0.2813 (3)	0.1059 (2)	4.67 (5)
O-6	0.7569 (3)	0.3778 (3)	0.4830 (2)	5.03 (5)
C-1	0.6516 (5)	0.6438 (4)	0.6835 (3)	4.20 (6)
C-2	0.7265 (4)	0.7898 (3)	0.5836 (2)	3.98 (6)
C-3	0.8525 (4)	0.7657 (3)	0.4588 (2)	3.31 (5)
C-4	0.8172 (4)	0.9305 (3)	0.3373 (2)	3.68 (5)
C-5	0.9266 (4)	0.9189 (3)	0.2043 (2)	3.14 (4)
C-6	0.8456 (4)	0.8078 (3)	0.1444 (2)	3.14 (4)
C-7	0.9429 (5)	0.8207 (3)	0.0037 (3)	4.29 (6)
C-8	0.9636 (5)	0.6462 (4)	−0.0033 (3)	4.92 (7)
C-9	0.9616 (4)	0.5313 (3)	0.1454 (3)	3.59 (5)
C-10	1.1666 (4)	0.3742 (3)	0.1928 (3)	3.67 (5)
C-11	1.1350 (5)	0.2541 (3)	0.3351 (3)	4.39 (6)
C-12	1.1643 (5)	0.3006 (4)	0.4575 (3)	4.75 (7)
C-13	0.9456 (4)	0.3697 (3)	0.5208 (2)	3.82 (5)
C-14	0.9758 (4)	0.4136 (3)	0.6453 (2)	3.95 (5)
C-15	1.1068 (4)	0.6791 (3)	0.4972 (2)	3.79 (5)
C-16	1.1406 (4)	0.5246 (3)	0.6274 (2)	4.01 (6)
C-17	0.6785 (6)	0.9296 (4)	0.6128 (3)	5.64 (9)
C-18	0.5845 (4)	0.8378 (3)	0.1454 (3)	4.41 (6)
C-19	1.3960 (4)	0.4201 (3)	0.1798 (3)	4.65 (7)
C-20	1.0570 (6)	0.2473 (4)	0.7649 (3)	5.68 (8)
WO	0.5019 (4)	1.2745 (3)	−0.0767 (2)	5.30 (5)

[a]Crystallographic numbering as in Figure 1.
[b]B_{eq} (Å^2) is the isotropic equivalent of the anisotropic temperature factor.

with EtOH. The extracts were filtered and evaporated under reduced pressure to leave an aqueous residue which was shaken successively with petroleum ether, CH_2Cl_2, and EtOAc. Separation of the CH_2Cl_2 extract (23.4 g) by vlc on Si gel using a gradient of CH_2Cl_2 and Me_2CO gave, in order of increasing polarity, two sterol fractions (by 60 MHz ^{1}H-nmr examination), 3.67 g and 2.31 g, an intermediate fraction that deposited a solid precipitate, and two very minor unidentified substances. The precipitate was recrystallized from Et_2O to yield **1**.

Sinulariolone [**1**].—Colorless prisms (0.70 g; 0.09%), mp 215–216°, $[\alpha]^{25}D$ −15.8° (*c*=0.634, EtOH); ir ν max (KBr) 3400–3200, 2900, 2850, 2700, 1720, 1700, 1620, 1240, 1140, 1040 cm^{-1}; uv λ max (EtOH) 214.1 nm (ε 8970); ^{1}H- and ^{13}C-nmr data, see Table 1; eims *m/z* 349 (M^+ −17, 2), 292 (6), 249 (4), 221 (6), 203 (6), 183 (6), 165 (7), 139 (13), 137 (11), 135 (15), 125 (21), 111 (56), 99 (29), 85 (31), 55 (29), 43 (100), 41 (37); cims *m/z* 349 (M^+ −17, 100), 331 (38), 313 (21), 295 (6), 292 (6), 287 (6), 285 (6), 249 (5), 221 (6), 203 (6), 183 (7), 165 (9), 149 (10), 139 (16), 137 (12), 135 (14), 125 (20), 111 (29), 99 (16), 95 (17), 85 (20), 69 (12), 55 (13), 43 (24); *anal.*, found C, 62.8, H, 8.9. $C_{20}H_{30}O_6 \cdot H_2O$, requires C, 62.5, H, 8.4.

Acetylation of sinulariolone [**1**].—Sinulariolone [**1**] (10 mg) and Ac_2O (50 μl) were dissolved together in pyridine (1 ml). The mixture was allowed to stand overnight, diluted with $CHCl_3$ (3 ml), and washed thoroughly with dilute AcOH. Evaporation of solvent gave the acetate **2** as a gum. ^{1}H-Nmr data, see Table 1.

X-RAY CRYSTALLOGRAPHIC DATA FOR SINULARIOLONE [**1**].[1]—$C_{20}H_{30}O_6 \cdot H_2O$, mol wt 384.5, triclinic, space group P_1, *a*=6.0405(4), *b*=8.7969(5), *c*=10.5384(7)Å, α 69.082(5), β 85.459(4), γ 74.113(5)°, V 502.99(6)Å^3, D_c 1.27 g cm^{-3}, Z 1, μCu 7.46 cm^{-1}. Crystal size 0.07 by 0.21 by 0.54 mm, 2θ max 140°, min and max transmission factors 0.75 and 0.95. The number of reflections was 1845 considered observed out of 1914 unique data. Final residuals R, R_w were 0.028, 0.040.

Structure determination.—Reflection data were measured with an Enraf-Nonius CAD-4 diffractometer in θ/2θ scan mode using nickel filtered copper radiation (λ 1.5418Å). Data were corrected for absorption. Reflections with $I>3\sigma(I)$ were considered observed. The structure was determined by direct phasing and Fourier methods. Hydrogen atoms bonded to oxygens were located in a difference Fourier, the remainder were included in calculated positions and all were assigned thermal parameters equal to those of the atom to which bonded. Positional and anisotropic thermal parameters for the non-hydrogen atoms were refined using full matrix least squares. Reflection weights used were $1/\sigma^2(F_o)$, with $\sigma(F_o)$ being derived from $\sigma(I_o)=[\sigma^2(I)+(0.04I)^2]^{1/2}$. The weighted residual is defined as $R_w=(\Sigma w\Delta^2/\Sigma wF_o^2)^{1/2}$. Atomic scattering factors were from International Tables for X-ray Crystallography (21). Structure solution was by MULTAN 80 (22) and refinement used BLOCKLS, a local version of ORFLS (23). ORTEP-II (24) running on a Macintosh IIcx was used for the structural diagram, and an IBM 3090 computer was used for calculations.

The structure and crystallographic atom numbering scheme are shown in Figure 1 and atomic parameters are recorded in Table 3.

ACKNOWLEDGMENTS

The authors are grateful to Mr. P. Alderslade of the Northern Territory Museum for his kind assistance in the identification of the specimen of *S. flexibilis* and to Mr. D.C. Craig of the School of Chemistry, The University of New South Wales for providing the X-ray crystallographic analysis. P.P.G. acknowledges the receipt of a grant from the UNESCO Regional Network for the Chemistry of Natural Products and financial support from the Network for the Chemistry of Biologically Important Natural Products (NCBINP), an activity of the International Development Programme of Australian Universities and Colleges, to undertake a research visit to Australia. P.P.G. also thanks De La Salle University for study leave.

LITERATURE CITED

1. B. Tursch, J.C. Braekman, D. Daloze, M. Herin, R. Karlsson, and D. Losman, *Tetrahedron*, **31**, 129 (1975).
2. M. Herin and B. Tursch, *Bull. Soc. Chim. Belg.*, **85**, 707 (1976).
3. A.J. Weinheimer, J.A. Matson, M.B. Hossain, and D. van der Helm, *Tetrahedron Lett.*, 2923 (1977).
4. Y. Kashman, M. Bodner, Y. Loya, and Y. Benayahu, *Isr. J. Chem.*, **16**, 1 (1977).

[1]Hydrogen coordinates, thermal parameters, bond distances and angles, and observed and calculated structure factors have been deposited with the Cambridge Crystallographic Data Centre and can be obtained upon request from Dr. Olga Kennard, University Chemical Laboratory, 12 Union Road, Cambridge CB2 1EZ, UK.

5. R. Kazlauskas, P.T. Murphy, R.J. Wells, P. Schönholzer, and J.C. Coll, *Aust. J. Chem.*, **31**, 1817 (1978).
6. K. Mori, S. Suzuki, K. Iguchi, and Y. Yamada, *Chem. Lett.*, 1515 (1983).
7. R. Karlsson, *Acta Cryst.*, **B33**, 2027 (1977).
8. R.S. Norton and R. Kazlauskas, *Experientia*, **36**, 276 (1980).
9. T. Kusumi, H. Uchida, M.O. Ishitsuka, H. Yamamoto, and H. Kakisawa, *Chem. Lett.*, 1077 (1988).
10. T. Hamada, T. Kusumi, M.O. Ishitsuka, and H. Kakisawa, *Chem. Lett.*, 33 (1992).
11. M. Maida, A.R. Carroll, and J.C. Coll, *J. Chem. Ecol.*, **19**, 2285 (1993).
12. L.A. Fontán, W.Y. Yoshida, and A.D. Rodriguez, *J. Org. Chem.*, **55**, 4956 (1990).
13. J.J. Morales, J.R. Espina, and A.D. Rodriguez, *Tetrahedron*, **46**, 5899 (1990).
14. L.A. Fontán and A.D. Rodriguez, *J. Nat. Prod.*, **54**, 298 (1991).
15. A. Bax and D.G. Davies, *J. Magn. Reson.*, **65**, 355 (1985).
16. D.T. Pegg, D.M. Doddrell, and M.R. Bendall, *J. Chem. Phys.*, **77**, 2745 (1982).
17. G.A. Morris and R. Freeman, *J. Am. Chem. Soc.*, **101**, 760 (1979).
18. W. Inman and P. Crews, *J. Org. Chem.*, **54**, 2526 (1989).
19. D.J. States, R.A. Haberkorn, and D.J. Ruben, *J. Magn. Reson.*, **48**, 286 (1982).
20. J.C. Coll and B.F. Bowden, *J. Nat. Prod.*, **49**, 934 (1986).
21. J.A. Ibers and W.C. Hamilton (Eds.), "International Tables for X-Ray Crystallography," Kynoch Press, Birmingham, UK, 1974, Vol. 4.
22. P. Main, "MULTAN 80," University of York, York, UK, 1980.
23. W.R. Busing, K.O. Martin, and H.A. Levy, "ORFLS," Oak Ridge National Laboratory, Oak Ridge, Tennessee, 1962.
24. C.K. Johnson, "ORTEP-II," Oak Ridge National Laboratory, Oak Ridge, Tennessee, 1976.

Received 29 December 1994