Journal of Natural Products
Vol. 50, No. 3, pp. 449-454, May-Jun 1987

STRICTAKETAL, A NEW TETRAPRENYLTOLUQUINOL WITH A HETEROTETRACYCLIC DITERPENE MOIETY FROM THE BROWN ALGA *CYSTOSEIRA STRICTA*

VINCENZO AMICO,* FRANCESCA CUNSOLO, MARIO PIATTELLI,

Dipartimento di Scienze Chimiche dell'Università di Catania, viale A. Doria 6, I-95125 Catania, Italy

GIUSEPPE RUBERTO,

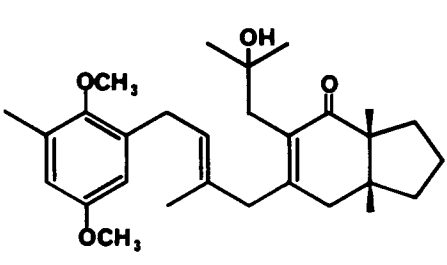
Istituto per lo Studio delle Sostanze Naturali di Interesse, Alimentare e Chimico-Farmaceutico del CNR, viale A. Doria 6, I-95125 Catania, Italy

and LUCIANO MAYOL

Dipartimento di Chimica delle Sostanze Naturali dell'Università di Napoli, via L. Rodinò 22, I-80188 Napoli, Italy

ABSTRACT.—A new metabolite of mixed biogenesis, strictaketal [**5**], has been isolated from the brown alga *Cystoseira stricta* and its structure with relative stereochemistry determined by spectral data, including two dimensional 2D-correlated nmr spectroscopy.

Chemical investigation of the algae belonging to the genus *Cystoseira* has resulted in the isolation of an array of metabolites with a tetraprenyltoluquinol structure (1-11) as, for example, cystalgerone [**1**], cystoketal [**2**], and balearone [**3**]. From *Cystoseira stricta* (Mont.) Sauv., a species widespread in Mediterranean waters, French workers have recently isolated a compound of this class, cystoseirol A [**4**], with a rearranged diterpenoid moiety (12). As part of our continuing research on the chemistry of Mediterranean algae, we wish to describe here the structure determination of a further metabolite from this same alga, strictaketal [**5**], possessing a regular diterpenoid portion.



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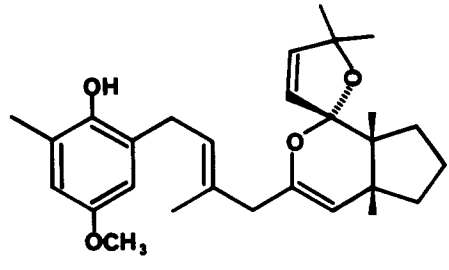

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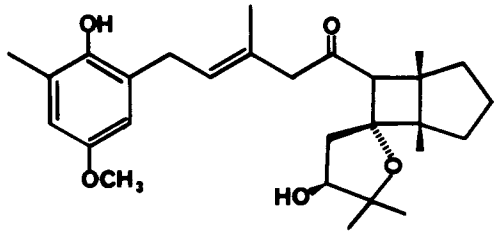

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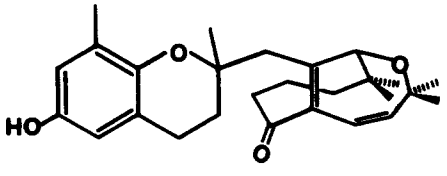

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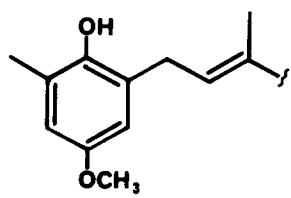
RESULTS AND DISCUSSION

Repeated chromatography of the $CHCl_3$ extract of the alga gave strictaketal [**5**] as an oil, $[\alpha]^{20}D=21.7°$, molecular formula $C_{28}H_{40}O_5$ (hrms). Uv absorptions at 215

(ϵ=10700) and 290 nm (ϵ=3690) suggested a hydroquinol chromophore, while a broad ir band at 3440 cm^{-1} was indicative of hydroxyl function(s). The ^{1}H-nmr spectrum displayed, in addition to an AB system (δ 6.57 and 6.53, J=3 Hz) assignable to two *meta*-coupled aromatic protons, signals for an aromatic methoxyl at δ 3.74, a methyl group on a benzene ring (δ 2.22) and a benzylic methylene at δ 3.34 (J=6.5 Hz). The latter was coupled with a vinyl proton at δ 5.36 (J=6.5 Hz) in turn allylically coupled with the vinyl methyl at δ 1.91. These data could be accommodated by partial structure **A** which is also consistent with the ^{13}C-nmr spectrum (Table 1). The presence in the mass spectrum of an ion at *m/z* 191 (base) confirmed this partial structure, while an intense fragment ion at *m/z* 189, explainable in terms of the oxonium structure **B**, indicated that the phenolic hydroxyl was located at C-1′ instead of C-4′. The rest of the ^{1}H-nmr spectrum of **5** provided little information because of the presence in the molecule of a large number of quaternary carbons. It consisted of a broad methylene singlet at δ 2.38, a 1H doublet at δ 1.69 (J=15.5 Hz) coupled with a doublet of doublets at δ 2.37 further coupled with a methine signal at δ 4.01, a methine singlet at δ 1.72, five methyl singlets (δ 1.91, 1.50, 1.18, 1.12, and 0.93), an OH signal (δ 4.87, D_2O-exchangeable), and a group of multiplets between δ 2.20 and 1.20, partly superimposed on other resonances, integrating for six protons altogether. Although complete analysis of this complex of signals was impossible (only one proton, H-10_a, was identifiable as a separate signal centered at δ 2.13), spin decoupling allowed its assignment to three adjacent methylenes not further coupled with the rest of the protons in the molecule.

A DEPT experiment identified the multiplicity of each ^{13}C-nmr resonance and in conjunction with two-dimensional one-bond ^{1}H-^{13}C correlation permitted the assignment of all the protonated carbons in the ^{13}C-nmr spectrum of **5**, except for C-8 and C-9. These two carbon signals (42.1 and 24.5 ppm) both correlated with methylene protons in the range 1.65-1.20. By analogy with model compounds (5), the former was assigned to C-8 and the latter to C-9. In any case, this information is not essential for the inference of the structure described below. The spectrum also includes the resonances for ten quaternary carbons, five of them in the sp^2 region and one (107.7 ppm) assignable to a carbon bearing two oxygen atoms.

Further insight into the structure of **5** was provided by 2D-long range ^{1}H-^{13}C shift correlation spectroscopy (Table 1). The presence of part structure **A**, already defined as discussed above, was readily confirmed by the correlation of C-1′ with Me-6′, H-3′, H-5′, and 2H-1; C-2′ with OH-1′ and 2H-1; C-3 with 2H-1; C-4′ with OMe and H-3′; C-5′ with Me-6′; C-6′ with Me-6′ and OH-1′; C-2 and C-3 with 3H-20 and 2H-4. Extension of this substructure to include all the carbons in the molecule and one more oxygen atom was possible on the basis of the following considerations. Long-range correlation of the resonance at 107.7 ppm with the protons at C-4 and C-6 identified C-5, which is also interrelated through an oxygen atom to the proton at C-14. The assignment of the ring junction carbons C-7 and C-11 followed from correlations of the former with protons H-6, 3H-19 (^2J), and 3H-18 (^3J), and of the latter with 3H-18 (^2J)



A

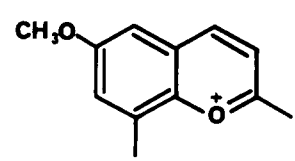


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TABLE 1. ^{1}H- and ^{13}C-nmr Data of Strictaketal [**5**][a]

Position	δ^{13}C	DEPT	δ^1H	J_{HH}	Long range correlations[b]
1′	146.1	C			Me-6′, 2H-1, H-3′, H-5′
2′	127.7	C			OH-1′, 2H-1
3′	113.1	CH	6.57	d 3	2H-1
4′	153.1	C			OMe, H-3′
5′	114.0	CH	6.53	d 3	Me-6′
6′	125.6	C			Me-6′, OH-1′
1	30.4	CH_2	3.34	d 6.5	
2	126.9	CH	5.36	bt 6.5	2H-4, 3H-20
3	133.0	C			2H-4, 3H-20, 2H-1
4	46.6	CH_2	2.38	bs	
5	107.7	C			2H-4, H-6, H-14
6	55.6	CH	1.72	s	3H-19
7	43.0	C			H-6, 3H-18, 3H-19
8	42.1	CH_2			
			1.65-1.20[c]		
9	24.5	CH_2			
		$H\text{-}10_a$	2.13[c]		
10	36.0	CH_2			3H-18
		$H\text{-}10_b$	1.25[d]		
11	52.4	C			3H-18, 3H-19
12	69.7	C			H-6, H-14, 3H-18
		$H\text{-}13_a$	2.37	dd 15.6, 6	
13	32.5	CH_2			
		$H\text{-}13_b$	1.69	d 15.6	
14	80.1	CH	4.01	d 6	3H-16, 3H-17
15	79.3	C			2H-13, 3H-16, 3H-17
16	29.0	CH_3	1.18	s	3H-17
17	22.6	CH_3	1.50	s	3H-16
18	19.0	CH_3	0.93	s	
19	16.9	CH_3	1.12	s	
20	18.4	CH_3	1.91	bs	
Me-6′	16.2	CH_3	2.22	s	
OMe	55.6	CH_3	3.74	s	
OH-1′			4.87	s	

[a]The ^{1}H- and ^{13}C-nmr spectra were run at 250 and 62.5 MHz, respectively, in $CDCl_3$ (ppm from TMS).

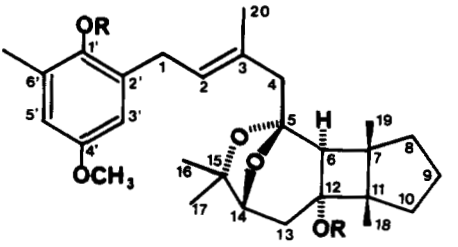
[b]Long range correlations were obtained by two experiments for optimum generation of polarization transfer with J=5.0 and 7.25 Hz, respectively.

[c]Complex multiplets.

[d]Overlapped.

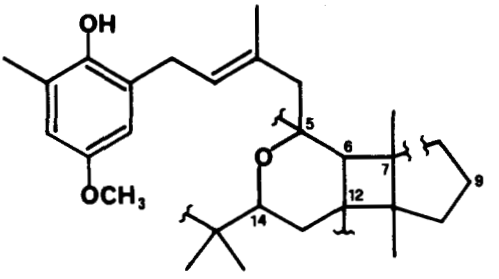
and 3H-19 (^3J). The oxygen-bearing quaternary carbon resonating at 69.7 ppm (C-12) was positioned through its correlations with H-6, 3H-18, and H-14. Moreover, C-14 was seen to correlate with 3H-16 and 3H-17, while C-15 was interrelated to the same protons and to 2H-13. Finally, correlation of C-10 with 3H-18 located one extreme of the three-methylene sequence. Thus, partial structure **C** could be written. To complete the structure, one oxygen of the ether type and one hydroxyl must be added to form a tetracyclic system, as the molecular formula of **5** implies nine degrees of unsaturation. Because C-8 must be necessarily linked to the single nonoxygen-bearing quaternary carbon still remaining (C-7), thus closing the cyclopentane ring, only three structures are to be considered, in which the hydroxyl is located in one of the positions 5, 12, or 15, the last oxygen being bonded to the other two carbons.

In order to make a choice among these possibilities, strictaketal [**5**] was converted into the diacetate **6**. Comparison of the ^{13}C-nmr spectrum of the latter with that of the



5 R=H
6 R=$COCH_3$

original compound (Table 2) clearly showed that the hydroxyl group is linked to C-12, thus leading unequivocally to structure **5**. The *E*-geometry of the double bond was indicated by the chemical shift (18.4 ppm) of the vinyl methyl in the ^{13}C-nmr spectrum, while the relative stereochemistry at C-5, C-6, C-7, C-11, C-12, and C-14 depicted in



C

structure **5** was deduced from nOe data (Table 3), which require the angular methyls and the protons H-13_a and H-14 to be on the same face of the molecule (Figure 1). Assignment of the relative configuration of the stereocenters at C-6, C-7, C-11, and C-12 is in agreement with the stereostructure of a related *Cystoseira* metabolite, balearone [**3**], which was determined by single-crystal X-ray analysis (5).

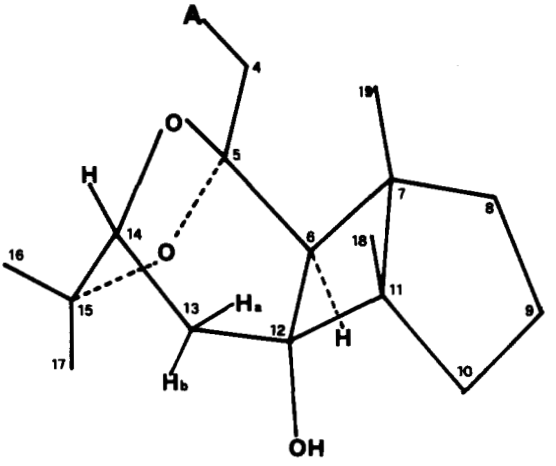


FIGURE 1. Stereostructure of strictaketal [**5**]

TABLE 2. Chemical Shift Differences in the ^{13}C nmr of Strictaketal [**5**] and its Diacetate [**6**]

	C-12	C-6	C-11	C-13	C-5	C-7	C-10	C-18	C-14	C-15
12-OH	69.7	55.6	52.4	32.5	107.7	43.0	36.0	19.0	80.1	79.3
12-OAc . . .	65.8	51.7	53.0	29.3	107.8	43.5	38.5	19.6	79.7	79.1
Δδ	3.9	3.9	−0.6	3.2	−0.1	−0.5	−2.5	−0.6	0.4	0.2

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Mass spectra were performed with direct inlet system at 70 eV on a Kratos MS-50S instrument. Ir and uv spectra were determined on Perkin-Elmer model 684 and model 330 spectrophotometers, respectively. ^1H- and ^{13}C-nmr spectra were measured at 250 and 62.5 MHz, respectively, on a Bruker AM-250 instrument. Chemical shifts are quoted in ppm (δ) relative to internal TMS. Optical rotations were determined with Perkin-Elmer 141 polarimeter. Preparative liquid chromatography (plc) was carried out on a Jobin-Yvon Miniprep-LC instrument.

TABLE 3. Results of nOeds Experiments on Strictaketal [**5**]

Signal irradiated	Signal enhanced	% Enhancement
Me-11 (δ 0.93 s) . .	H-13$_a$ (δ 2.37 dd)	18
Me-7 (δ 1.12 s) . . .	H-4 (δ 2.38 bs)	13
	H-14 (δ 4.01 d)	5
H-14 (δ 4.01 d) . . .	H-13$_a$ (δ 2.37 dd)	12
	H-13$_b$ (δ 1.69 d)	10
	H-16 (δ 1.18 s)	11
	H-17 (δ 1.50 s)	7
	H-18 (δ 0.93 s)	4

ISOLATION OF STRICTAKETAL [**5**].—*C. stricta* (voucher specimen deposited at the Herbarium of the Department of Botany, Palermo, Italy) was collected on rocks at about 1 m depth in April 1984, at Portopalo, Sicily. It was shade dried and powdered (1.7 kg) and then extracted three times with CH_2Cl_2 at room temperature with continuous stirring. The extracts were pooled and evaporated to give a dark green oil (40 g). The crude extract was applied to an open column (4×120 cm) of Si gel using eluents of increasing polarity from hexane to Et_2O. Fractions of 200 ml were collected, and those exhibiting similar tlc profiles were combined. Fractions 70-85 were pooled and subjected to successive plc (LiChroprep Si-60) using as eluent CH_2Cl_2-Et_2O (97:3) to yield **5** (816 mg, 0.048% dry weight); $[\alpha]^{20}(\lambda)+21.7°$ (589), +22.4° (578), +26.5° (546), +49.6° (436), +90.1° (365) (c 0.9 in EtOH); ir ν max (film) 3440, 1605 cm^{-1}; uv λ max (EtOH) 290 nm (ϵ=3690), 215 (ϵ=10700); hrms 456.2880 (M^+), calcd for $C_{28}H_{40}O_5$ 456.2875; ms *m/z* (%) 456 (23), 438 (5), 420 (7), 301 (65), 251 (33), 231 (44), 206 (23), 192 (26), 191 (100), 190 (26), 189 (67), 176 (28), 168 (48), 155 (23), 151 (56), 150 (56), 137 (44), 127 (86), 113 (46), 111 (26), 109 (32), 96 (56), 95 (51), 81 (49), 71 (37), 69 (28), 67 (23), 59 (21), 55 (30), 43 (53), 41 (35).

ACETYLATION OF **5**.—To a solution of **5** (50 mg) in CH_2Cl_2 (3 ml) was added acetyl chloride (0.1 ml) and *N,N*-dimethylaniline (0.2 ml). The mixture was stirred for 20 h at room temperature. Evaporation in vacuo gave an oily residue which was subjected to plc (LiChroprep Si-60) using as eluent hexane-Et_2O (7:3) to give **6** (23 mg): ir ν max (film) 1765, 1740 cm^{-1}; ^1H nmr (250 MHz, TMS, δ in $CDCl_3$) 6.64 and 6.60 (2H, AB system, J=3 Hz, H-3′ and H-5′), 5.32 (1H, t, J=7.5 Hz, H-2), 3.94 (1H, d, J=5.5 Hz, H-14), 3.78 (3H, s, OMe), 3.19 (2H, d, J=7.5 Hz, H-1), 2.52 (1H, dd, J=17, 5.5 Hz, H-13$_a$), 2.37 (2H, bs, H-4), 2.31 (3H, s, Me-6′), 2.11 (3H, s, Ac), 2.07 (1H, d, J=17 Hz, H-13$_b$), 2.06 (1H, s, H-6), 2.03 (3H, s, Ac), 1.83 (3H, s, H-20), 1.30 and 1.16 (6H, 2s, H-16 and H-17), 1.14 and 1.11 (6H, 2s, H-18 and H-19); ^{13}C nmr (65.5 MHz, TMS, ppm in $CDCl_3$) 170.1 (s, $OCOCH_3$), 169.1 (s, $OCOCH_3$), 157.3 (s, C-4′), 141.8 (s, C-1′), 134.2 (s, C-2′), 131.6 (1, C-3), 131.2 (s, C-6′), 127.0 (d, C-2), 113.8 (d, C-5′), 113.1 (d, C-3′), 107.8 (s, C-5), 79.7 (d, C-14), 79.1 (s, C-15), 65.8 (s, C-12), 55.5 (q, OMe), 53.0 (s, C-11), 51.7 (d, C-6), 46.4 (t, C-4), 43.5 (s, C-7), 43.1 (t, C-8), 38.5 (t, C-10), 29.5 (t, C-13), 29.4 (t, C-1), 29.1 (q, C-16), 24.7 (t, C-9), 22.5 (q, C-17 and q, $OCOCH_3$), 20.4 (q, $OCOCH_3$), 19.6

(q, C-18), 18.5 (q, C-20), 17.4 (q, C-19), 16.6 (q, Me-6′); hrms 540.6993 (M^+), calcd for $C_{32}H_{44}O_7$ 540.6998.

ACKNOWLEDGMENTS

This study was financially supported by the Consiglio Nazionale delle Ricerche, Rome, under the scheme "Progetto Finalizzato per la Chimica Fine e Secondaria." We wish to thank Dr. Placido Neri for technical assistance.

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Received 6 October 1986