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STRUCTURE AND CONFORMATION OF PACHYLACTONE, A NEW DITERPENE ISOLATED FROM THE BROWN ALGA, PACHYDICTYON CORIACEUM

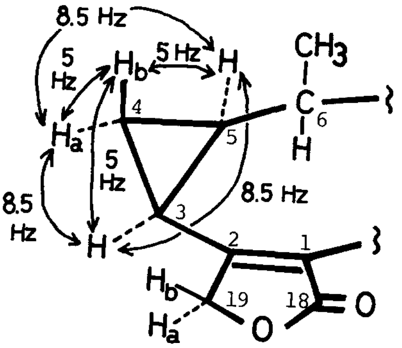
Midori Ishitsuka, Takenori Kusumi, Hiroshi Kakisawa*,
Yoshiyuki Kawakami+, Yasushi Nagai+, and Tadashi Sato+
Department of Chemistry, The University of Tsukuba,
Sakura-mura, Ibaraki 305, Japan
+Tsukuba Research Laboratory, Eisai Company Co., Ltd.,
Toko-dai, Toyosato, Niihari-gun, Ibaraki 300-26, Japan

Abstract: A new diterpene, pachylactone (1), was isolated from the brown alga, Pachydictyon coriaceum, and its structure together with the stereochemical features was elucidated by spectral analyses.

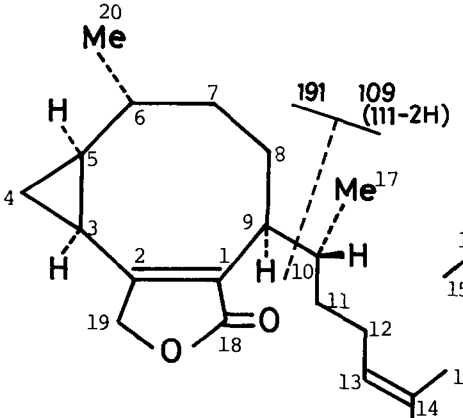
The brown alga, Pachydictyon coriaceum, has been revealed to contain various type of new diterpenes such as acetyldictyol C,[1] acetylsanadaol,[2] and acetylcoriacenone,[3] as well as the known diterpenes, dictyolactone[1,4] and dictyodial.[1,4] By repeated column chromatography on silica gel of the methanol extract of the alga, followed by HPLC (TSK GEL LS-410K, MeOH) separation, a new compound, which was designated as pachylactone, was obtained as an oil (4 mg from 30 g of the methanol extract), and this paper deals with the elucidation of the structure and stereochemistry of pachylactone.

Pachylactone, $C_{20}H_{30}O_2$ (M^+, m/z 302), $[\alpha]_D^{25}$ -23.3° (c 0.18, $CHCl_3$), exhibits IR bands at 1755 (s) and 1660 (w) cm^{-1}, and ^1H-NMR signals (90 MHz) centered at δ 4.60 (2H,ABq,J=16 Hz), which, coupled with UV maximum at 228 nm (ε 11700), indicate the presence of an α,β-unsaturated γ-lactone. The fragments at m/z 191 (100%) and 109 (44%) suggest that 1,5-dimethyl-4-hexen-1-yl group, the side chain which is frequently encountered in the diterpenes from the Dictyotaceae sea weeds,[1-4] is included in pachylactone. Its ^{13}C-NMR spectrum (Table 2) shows a series of signals, the chemical shifts of which correspond well to those reported for the side chain carbons.[1-4] The presence of a cyclopropane ring in pachylactone is recognized by the multiplet at δ 0.11 (1H) appearing in the ^1H-NMR spectrum (90 MHz).

Analysis of the 400 MHz ^1H-NMR spectrum (Table 1) allowed us to propose the structure 1 for pachylactone. The upfield signal ascribable to a cyclopropane methylene proton (4-H_b) appears as a quartet (J=5 Hz) at δ 0.11. The coupling pattern shows that this proton is equally coupled with three protons, 4-H_a (J^{gem}=5 Hz), 3-H (J^{trans}=5 Hz), and 5-H (J^{trans}=5 Hz). The other methylene proton signal (4-H_a) appears at δ 0.91 as a double triplet (J^{gem}=5 Hz; J^{cis}_{4a-3}=J^{cis}_{4a-5}=8.5 Hz). From these properties, it is obvious that the cyclo-



propane ring is cis-disubstituted.[5] Decoupling experiments showed that two other cyclopropane protons exhibit signals at δ 1.0 and 1.7. The downfield chemical shift of the latter suggests that the cyclopropane ring is connected with an unsaturated moiety, the α,β-unsaturated γ-lactone. By means of 2D-correlation spectroscopy (COSY),[6] together with decoupling works, a tertiary carbon (C-6) possessing a methyl group is revealed to be adjacent to the other side of the cyclopropane ring. Surprisingly, the proton (6-H) on this tertiary carbon is highly shielded up to δ 0.85, indicating that this proton orients above the plane formed by a carbon-carbon double bond (C_1=C_2). Detection of a 5% NOE between 4-H_b (δ 0.11) and 19-H_b (δ 4.46) settled the position of the lactonic carbonyl at C-18 (not at C-19).



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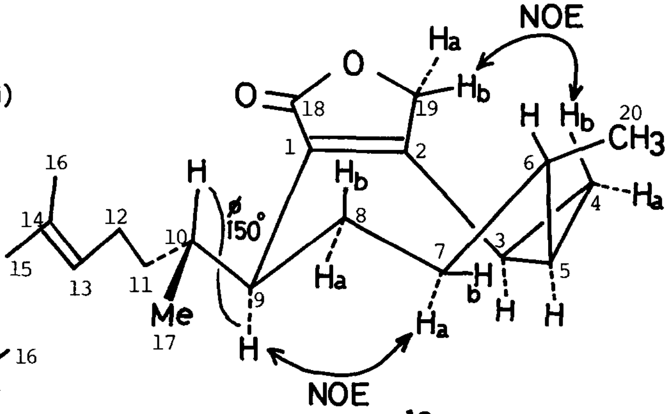


1a

The downfield triplet (J=9 Hz) at δ 2.54 is ascribable to an allylic methine (9-H). Irradiation at this signal simplified the multiplets at δ 1.45 (8-H_b) and 2.33. Inversely, irradiation at the latter multiplet (δ 2.33) simultaneously changed the triplet at δ 2.54 into a doublet, and a doublet due to a methyl (17-Me; δ 0.95) into a singlet. These facts show that the multiplet at δ 2.33 is assignable to 10-H. This unusual downfield chemical shift of 10-H, and also a relatively large coupling constant (9 Hz) between 10-H and 9-H are best interpreted by assuming that the rotation about C_9-C_{10} axis of the side chain would be restricted, and the side chain would take the conformation, in which 10-H has to be located close to the carbonyl group (C-18), and, at the

Table 1. ^{1}H-NMR chemical shifts of pachylactone (1).

position No.		
3	δ 1.7	(m)
4a	0.91	(dt,J=5,8.5 Hz)
4b	0.11	(q,J=5 Hz)
5	1.0	(dtd,J=10,8.5,5 Hz)*
6	0.85	(m)
7a	1.54	(m)
7b	1.7	(ddd,J=12,7,2 Hz)*
8a	2.0	(m)
8b	1.45	(m)
9	2.54	(t,J=9 Hz)
10	2.33	(m)
11	1.32	(m)
11	1.05	(m)
12	1.95	(2H,m)
13	5.08	(bt,J=7 Hz)
15	1.66	(3H,s)
16	1.58	(3H,s)
17	0.95	(3H,d,J=7 Hz)
19a	4.68	(d,J=17 Hz)
19b	4.46	(d,J=17 Hz)
20	1.00	(3H,d,J=7 Hz)

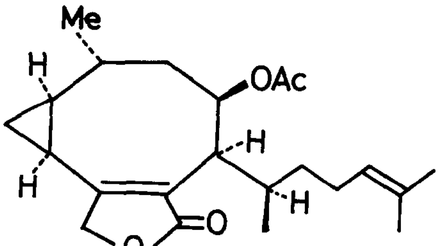
*Coupling pattern was determined by J-resolved 2D-spectroscopy.

Table 2. ^{13}C-NMR chemical shifts of 1 and isoacetoxycrenulatin (2).

carbon No.	1	2
1	δ 131.1	δ 131.3
2	160.3	162.4
3	13.6*	13.2
4	8.7	7.9
5	25.5*	25.7
6	35.7	29.8
7	39.0	44.8
8	30.1	70.9**
9	43.0	46.8
10	32.0	30.1
11	35.4	35.6
12	25.5	26.4
13	124.9	124.7
14	135.0	131.5
15	25.7	24.7
16	17.8	17.5
17	17.7	18.0
18	174.0	173.8
19	71.7	71.3
20	23.3	23.7

*Assignment was confirmed by heterospin selective decoupling works. **Carbon bearing an acetoxyl group.

same time, the dihedral angle formed by 9-H and 10-H has to be around 150°. A significant NOE was detected for 9-H by irradiating at 7-H_a (δ 1.54) (NOE difference spectrum). From the considerations of all these properties, the conformation of pachylactone, as well as the relative configurations at C-6 and C-9, was deduced as in 1a. The unusual upfield chemical shift of 6-H (δ 0.85) is well interpreted by this conformation; the proton situates not only above the plane of $C_1=C_2$, but also above the cyclopropane ring.[7] Molecular models show that the dihedral angles formed by 9-H and each of 10-H, 8-H_b, and 8-H_a are 150°, 170°, and 75°, respectively, thus, verifying the triplet nature of 9-H. The coupling constant between 5-H and 6-H was



2

determined to be 10 Hz by J-resolved 2D-NMR spectroscopy.[6] This magnitude is quite reasonable, since these protons are in the anti-coplanar relationship in 1a. Detection of NOE's between 19-H_b and 4-H_b (2.2 Å) and also between 7-H_a and 9-H (2.3 Å) is a good evidence for this conformation.

Recently, the structure elucidation of isoacetoxycrenulatin (2) (except for stereochemistry) has been reported.[8] The present diterpene, pachylactone (1), exhibits the ^{13}C-NMR spectrum closely resembling that of 2 (Table 2), which indicates that these diterpenes have the same carbon framework, crenulatane.[9] On the basis of the ^{1}H-NMR data reported for isoacetoxycrenulatin (2),[8] coupled with the considerations of the proposed conformation (1a) of pachylactone, the stereochemistry of isoacetoxycrenulatin was deduced to be as illustrated in 2.

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