DISSESSATION

STUDIES ON METABOLITES OF
THE SARGASSACEAE AND DICTYOTACEAE BROWN ALGAE

BY

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INTRODUCTION

Plants are in very close contact with human being, and they are inevitable for our life, not only because they afford us foods, woods, and other useful materials, but also because they produce such constituents that are used as medicines, insecticides, and other biologically significant compounds. A lot of studies have been done for the constituents of terrestrial plants, but very few attention has been paid toward marine plants, seaweeds. Simple reason of this is that marine plants grow in the sea, where man cannot go without special devices, and, moreover, not much information about their physiology has been obtained in contrast to that about terrestrial plants. However, owing to recent findings that marine organisms produce a variety of compounds quite different from those of terrestrial organisms, and some of the compounds exhibit significant biological and pharmaceutical properties, increasing interests have been focused on the ingredients of seaweeds, marine mollusks, and microorganisms.

This thesis describes the structure determination of the constituents of the brown algae belonging to Sargassaceae and Dictyotaceae. The seaweeds are very commonly seen along the Japanese coasts, and I could isolate a plenty of new compounds from them. Most of them have unique structures that have never seen in terrestrial plants.

The first chapter deals with the structure determination
of the constituents of Sargassaceae seaweeds. This chapter is divided into four sections according to biogenetical types of the compounds, followed by experimental parts.

The second chapter describes the isolation and the structure determination of the diterpenoids of Dictyotaceae algae. This chapter is divided into seven sections and arranged in the same manner as in the first chapter. In the final section of them, the biogenetic pathways of the diterpenoids isolated from the Dictyotaceae brown algae are proposed.
CHAPTER I

STUDIES ON METABOLITES OF THE SARGASSACEAE
BROWN ALGAE
Brown algae belonging to the family Sargassaceae are among the most abundant seaweeds growing along Japanese coast. I investigated the constituents of ten species of this family (Table 1), collected at Awakominato, Chiba, and isolated a number of new compounds including plastoquinones, linear terpenoids, and a new type of glyceride. This chapter deals with the structures of these compounds.

Table 1. Sargassum spp.

- **S. serratifolium** (nokogirimoku)
- **S. tortile** (yoremoku)
- **S. micracanthum** (togemoku)
- **S. fulvellum** (hondawara)
- **S. piluliferum** (mametawara)
- **S. giganteifolium** (oobanokogirimoku)
- **S. ringgoldianum** (oobamoku)
- **S. sagamianum** (nezimoku)
- **S. hemiphyllum** (isomoku)
- **S. yendoi** (endoumoku)
I-A Components of *Sargassum serratifolium*¹)

Methanolic extraction of the fresh brown alga *S. serratifolium*, followed by chromatographic separation afforded three new compounds, sargaquinoic acid (1), sargaquinal (2), and sargachromenol (6).

**Sargaquinoic acid (1),** oil, C_{27}H_{36}O_{4}, shows the following spectral properties: \( \lambda_{\text{max}}(\text{EtOH}) 251 \text{ nm} (\epsilon 14500) \); \(^1\)H-NMR(CDCl\(_3\))\(\delta\) 6.56 (1H, dq, J=2, 0.5 Hz), 6.46 (1H, dt, J=2, 0.5 Hz), 6.02 (1H, t, J=6 Hz, 10-H), 5.16 (3H, m, 2-&, 6-&, 14-H's), 3.14 (2H, brd, J=7 Hz, 1-H), 2.62 (2H, q, J=7 Hz, 9-H), 2.04 (3H, brs, quinone Me), 1.68 (3H, brs, 3-Me), 1.63, 1.61, 1.59 (each 3H, brs, 7-&, 15-&, 15-Me's); IR(CHCl\(_3\)): 3400-2500, 1680, 1650, 1610 cm\(^{-1}\). The \(^{13}\)C-NMR (CDCl\(_3\)) data of sargaquinoic acid showed the presence of five methyls (\(\delta\) 15.9, 16.0, 16.1, 17.7, 25.7), seven methylenes (\(\delta\) 26.4, 27.6, 27.9, 28.2, 34.6, 39.1, 39.6) and six trisubstituted olefins (singlets at \(\delta\) 130.7, 132.2, 134.6, 139.8, 145.9, 148.5 and doublets at \(\delta\) 118.1, 123.5, 124.6, 132.3, 133.2, 145.6), together with benzoquinone carbonyls (\(\delta\) 188.0) and a carboxyl carbon (\(\delta\) 173.5). The coupling constant (2 Hz) of the two quinone protons in \(^1\)H-NMR suggested the meta orientation of the methyl group and the C\(_{20}\)-side chain. The E-configurations of the double bonds at C\(_2\)-C\(_3\) and C\(_6\)-C\(_7\) were determined by the chemical shifts of the two vinyl methyls,²) and that at C\(_{10}\)-C\(_{11}\) by comparison of the chemical shifts of the olefinic proton at C\(_{10}\) and C\(_9\)-methylene.
protons with those reported\textsuperscript{3}) for E- and Z-2-methyl-2-pentenoic acids. The mass spectrum of 1 showed the base peak at m/e 175 due to the fragment (A), typical of the compounds such as plastoquinones and ubiquinones. The fragments (B) and (C) settled the position of the carboxyl group at C-11.

\textbf{Sargaquinal (2), oil, }C_{27}H_{36}O_3, \lambda_{\text{max}}(\text{EtOH}) 250 \text{ nm (} \varepsilon 15000 \text{)}, \text{IR(CHCl}_3): 1675, 1650 \text{ cm}^{-1}\text{ exhibited the }{^1}\text{H-NMR spectrum similar to that of 1. From the molecular formula and a sharp singlet at } \delta 9.36 \text{ in the spectrum, sargaquinal was considered to have an aldehyde function instead of the carboxyl group of 1. Hence, conversion of 1 into sargaquinal was attempted (Figure 1). Treatment of 1 with zinc-acetic anhydride yielded diacetate (3), which was reduced with excess lithium aluminum hydride. The resulting hydroquinone was}
Figure 1.

1. $\text{Zn/AC}_2\text{O}$

2. $\text{LiAlH}_4$

3. $\text{CrO}_3\cdot\text{pyr. HCl}$
smoothly oxidized by air on standing to afford 4, the primary hydroxyl group of which was oxidized with chromium oxide-pyridine hydrochloride complex. The mass spectrum of the derived aldehyde 5 was identical with that of sargaquinal (2), but the IR and $^1$H-NMR spectra were different from those of 2; in the $^1$H-NMR spectrum of 5, the aldehyde and 9-C methylene protons appeared at δ 10.06 and 2.65, respectively, while the corresponding aldehyde and methylene protons of sargaquinal (2) were observed at δ 9.36 and 2.45. These facts indicated that the configurations of the double bonds at 10-C of 5 and 2 are $E$ and $Z$, respectively.

![Structure of 2](attachment:image.png)

Sargachromenol (6), oil, C$_{27}$H$_{36}$O$_4$, gives the following data: $\lambda_{max}$(MeOH) 263 (ε 4900) and 332 nm (ε 2770); IR(CHCl$_3$): 3600, 3500-2500, 1680, 1590 cm$^{-1}$; $^1$H-NMR(C$_6$D$_6$) δ 6.35 (1H, d, J=2 Hz), 6.25 (1H, d, J=2 Hz), 6.11 (1H, d, J=10 Hz), 5.90 (1H, t, J=7 Hz), 5.31 (1H, d, J=10 Hz), 5.20 (2H, brt, J=6 Hz), 2.68 (2H, q, J=7 Hz), 2.15 (3H, s), 1.68 (3H, s), 1.56 (6H, s), 1.30 (3H, s). Although sargachromenol (6) has an asymmetric center, it shows no optical activity. When a dilute alcoholic solution of sargaquinoic acid (1) was allowed to stand at room tempera-
ture for one week, 1 was quantitatively converted into sargachromenol. Sargachromenol (6) must therefore be an artifact which was formed during the extraction process with methanol.
Components of Sargassum tortile

The ether-soluble material of the methanol extract of fresh S. tortile, collected at Awa-kominato, Chiba, was fractionated by flash chromatography using hexane-ethyl acetate (1:1). Repeated preparative TLC and HPLC of the resulting fractions afforded seven new compounds, 7, 11, 13, 15, 16, 17, and 18 (Figure 2), spectral properties of which are listed in Table 2 and 3.

The major component, which was named as sargatetraol (7), afforded tetraacetate (8). Presence of an α-glycol moiety was deduced from the $^1$H-NMR spectra of 7 and 8. Treatment of 7 with periodic acid in dry ether yielded geraniol (10) [IR(CCl$_4$) 1675 cm$^{-1}$; $^1$H-NMR(CDCl$_3$) δ 10.08 (1H, d, J=8 Hz), 5.90 (1H, d, J=8 Hz), 5.1 (1H, m), 2.15 (3H, s), 1.67 (3H, s), 1.59 (3H, s)] and the quinone (9) [IR(CCl$_4$) 1690, 1655, 1610 cm$^{-1}$; $^1$H-NMR(CDCl$_3$) δ 9.48 (1H, s), 6.62 (1H, m), 6.50 (1H, m), 6.50 (1H, t, J=7 Hz), 5.26 (1H, t, J=7 Hz), 3.17 (2H, d, J=8 Hz), 2.07 (3H, d, J=1.5 Hz), 1.76 (3H, s), 1.70 (3H, s)]. The production of these aldehydes settled the position of the two hydroxy groups at 8 and 9-C. The chemical shifts of 3-Me protons (δ 2.15) of 10 and the aldehyde proton (δ 9.48)$^{1,3}$ of 9 were consistent with the E,E-configurations of 6 and 10-C double bonds of 7. The configuration of 2-C double bond was determined to be E from the upfield chemical shifts$^5$ of the signals (δ 15.6, 16.1, 16.8, 17.6) due to 3, 7, 11 and 15 (trans to the olefin proton)
Figure 2.

7; R=H, 8; R=Ac

11; R=H, 12; R=Ac

13; R=H, 14; R=Ac

15

16

17

18

19

20
Table 2.
Spectral and physical properties of the compounds isolated from *S. tortile* and their derivatives.

<table>
<thead>
<tr>
<th></th>
<th>[α]_D</th>
<th>IR (cm⁻¹)</th>
<th>UV (nm)</th>
<th>NMR (δ)</th>
<th>MS (m/e)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(CHCl₃)</td>
<td>(CCl₄)</td>
<td>(ε, EtOH)</td>
<td>(CCl₄)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3610, 3600-3100,</td>
<td>290 (2840)</td>
<td>1.57 (6H, s), 1.63 (9H, s), 2.12 (3H, s),</td>
<td>410 (M-H₂O), 408 (M-2H-H₂O), 392 (M-3H₂O), 323 (c-2H₂O), 275 (b), 175 (a-2H), 69 (d)</td>
</tr>
<tr>
<td>7</td>
<td>c=0.47</td>
<td>1210, 1180, 1140</td>
<td></td>
<td>3.12 (2H, d, J=7 Hz), 0.87 (1H, d, J=8Hz),</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>4.31 (1H, t, J=8 Hz), 5.0-5.4 (4H, m),</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6.44 (2H, s)</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>+31.1°</td>
<td>1765, 1740, 1245,</td>
<td>260 (588)</td>
<td>1.56; 1.60; 1.65; 1.73; 1.94; 1.97; 2.11;</td>
<td>536 (M-CH₃COOH), 494 (536-C₂H₂O), 476 (M-2CH₃COOH),</td>
</tr>
<tr>
<td></td>
<td>c=0.54</td>
<td>1225, 1210, 1170</td>
<td></td>
<td>2.19, 2.24 (each 3H, s), 3.16 (2H, d, J=7 Hz),</td>
<td>434 (476-C₂H₂O), 401 (b), 359 (b-C₂H₂O), 317 (b-2C₂H₂O)</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>4.9-5.3 (3H, m), 5.11 (1H, d, J=8Hz),</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>5.5 (1H, m), 5.66 (1H, dd, J=8, 10 Hz),</td>
<td></td>
</tr>
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<td></td>
<td></td>
<td></td>
<td>6.77 (2H, ABq, J=3 Hz), 1.65 (3H, s)</td>
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<tr>
<td>11</td>
<td>-12.8°</td>
<td>3610, 3600-3200</td>
<td>290 (2470)</td>
<td>1.58 (3H, s), 1.62 (3H, s), 1.66 (9H, s),</td>
<td>412 (M), 410 (M-2H), 394 (N-H₂O), 392 (410-H₂O),</td>
</tr>
<tr>
<td></td>
<td>c=0.89</td>
<td></td>
<td></td>
<td>2.10 (3H, s), 3.18 (2H, d, J=7 Hz), 4.40</td>
<td>325 (b-H₂O), 257 (a-2H)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(1H, q, J=7 Hz), 5.0-5.3 (4H, m), 6.36</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(2H, ABq, J=3 Hz)</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>+7.36°</td>
<td>1765, 1730, 1370,</td>
<td>262 (605)</td>
<td>1.59; 1.67; 1.67; 1.69; 1.70; 1.91; 2.12;</td>
<td>478 (M-CH₃COOH), 436 (478-C₂H₂O), 409 (b-CH₃COOH),</td>
</tr>
<tr>
<td></td>
<td>c=1.10</td>
<td>1240, 1210, 1170</td>
<td></td>
<td>2.19, 2.24 (each 3H, s), 3.17 (2H, d, J=7 Hz),</td>
<td>394 (436-C₂H₂O), 301 (a-C₂H₂O), 69 (a)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5.0-5.3 (4H, m), 5.60 (1H, q, J=8Hz)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>6.70 (2H, ABq, J=2 Hz)</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>+3.51°</td>
<td>3610, 3600-3200</td>
<td>290 (1950)</td>
<td>1.23 (3H, s), 1.57 (6H, s), 1.65 (6H, s),</td>
<td>410 (M-2H), 392 (410-H₂O), 327 (c-2H), 325 (d-H₂O),</td>
</tr>
<tr>
<td></td>
<td>c=0.57</td>
<td></td>
<td></td>
<td>2.11 (3H, s), 2.66 (2H, br.s), 3.20 (2H, d, J=7 Hz), 4.8-5.6 (5H, m), 6.36 (2H, br.s)</td>
<td>323 (325-2H), 257 (b-2H), 175 (a-2H)</td>
</tr>
</tbody>
</table>
Table 3.
Spectral and physical properties of the compounds isolated from S. tortile and their derivatives.

<table>
<thead>
<tr>
<th>[α]_D (CHCl_3)</th>
<th>IR (cm⁻¹) (CCl_4)</th>
<th>UV (nm) (ε, EtOH)</th>
<th>NMR (δ) (CCl_4)</th>
<th>MS (m/e)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>+3.17° c=0.82</td>
<td>3600, 1765, 1370, 1230, 1170, 975</td>
<td>end absorption</td>
<td>1.18, 1.57, 1.57, 1.66, 1.66, 2.11, 2.19, 2.24 (each 3H, s), 2.65 (2H, br.s), 3.16 (2H, d, J=7 Hz), 4.9–5.5 (5H, m), 6.75 (2H, AB, J=3 Hz)</td>
<td>478 (M-H₂O), 413 (c), 371 (c-C₆H₅OH), 329 (c-C₂H₂O), 175 (a-2H-C₂H₂O)</td>
</tr>
<tr>
<td>+2.68 c=0.56</td>
<td>1655, 1615, 1295, 1100</td>
<td>253 (14700)</td>
<td>1.60 (6H, s), 1.65 (9H, s), 2.05 (3H, d, J=1.5 Hz), 3.10 (2H, d, J=8 Hz), 3.12 (3H, s), 3.88 (1H, q, J=8 Hz), 4.9–5.2 (4H, m), 6.40 (1H, br.m), 6.50 (1H, br.m)</td>
<td>424 (M), 392 (M-CH₃), 257 (c), 175 (b), 167 (d), 135 (a), 69 (e)</td>
</tr>
<tr>
<td>0 c=0.83</td>
<td>1655, 1615, 1295, 1075, 980</td>
<td>253 (15800)</td>
<td>1.16 (3H, s), 1.58 (6H, s), 1.65 (6H, s), 2.04 (3H, d, J=1.5 Hz), 3.70 (2H, d, J=5 Hz), 3.07 (3H, s), 3.10 (2H, d, J=8 Hz), 5.0–5.5 (5H, m), 6.39, 6.50 (each 1H, br.m)</td>
<td>424 (M), 392 (M-CH₃), 341 (d), 257 (c), 175 (b), 135 (a), 69 (e)</td>
</tr>
<tr>
<td>-15.5° c=0.39</td>
<td>3600–3300, 1655, 1630, 1615</td>
<td>253 (13100)</td>
<td>1.58 (6H, s), 1.61 (3H, s), 1.65 (6H, s), 2.04 (3H, d, J=1.5 Hz), 3.09 (2H, d, J=8 Hz), 3.71 (1H, d, J=8 Hz), 4.15 (1H, t, J=8 Hz), 5.0–5.4 (4H, m), 6.45, 6.53 (each 1H, br.m)</td>
<td>426 (M), 410 (M+2H-H₂O), 273 (c), 175 (b), 137 (a+2H), 69 (d)</td>
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<tr>
<td>-7.75° c=0.40</td>
<td>3600–3300, 1650, 1630, 1615</td>
<td>255 (13400)</td>
<td>1.60 (9H, s), 1.66 (6H, s), 2.01 (6H, s), 3.09 (2H, d, J=8 Hz), 3.71 (1H, d, J=8 Hz), 4.14 (1H, t, J=8 Hz), 5.0–5.4 (4H, m), 6.44 (1H, finely splitted triplet)</td>
<td>440 (M), 424 (M+2H-H₂O), 422 (M-H₂O), 287 (c), 189 (b), 151 (a+2H), 69 (d)</td>
</tr>
<tr>
<td>1650, 1610, 1290, 915</td>
<td>252 (12400)</td>
<td>1.59 (9H, s), 1.66 (6H, s), 2.05 (3H, d, J=1.5 Hz), 3.12 (2H, d, J=8 Hz), 5.1 (4H, m), 6.42 (1H, br.m), 6.53 (1H, br.m)</td>
<td>396 (M+2H), 394 (M), 325 (e), 257 (c), 175 (b), 137 (d), 135 (a), 69 (e)</td>
<td></td>
</tr>
</tbody>
</table>

*Letters a,b,c,d,e,f correspond to the fragments depicted in the Figure.*
methyls, in the $^{13}\text{C}-\text{NMR}$ spectrum of 7. The structure was further confirmed by the following transformation. Oxidation of 7 with silver oxide in ether afforded the quinone 17, which was also isolated from this alga as a minor component (vide infra). When the synthesized quinone 17 was heated in pyridine, it changed into the chromenol (20) in a good yield. This chromenol and its triacetate (acetic anhydride-pyridine) exhibited the same spectral and chiloptical properties as those of sargatriol (20), which has been reported to be a constituent of this alga, although the synthesized chromenol (20) was seemingly a mixture of epimers at 3-C.

From the fraction slightly less polar than that containing 7, two hydroquinone isomers, 11 and 13, were obtained. Acetylation of 11 and 13 with acetic anhydride-pyridine afforded the triacetate (12) and the diacetate (14), respectively, suggesting the presence of a secondary hydroxyl on 11 and a tertiary hydroxyl in 13. The position of the hydroxy groups of these compounds was determined on the basis of their mass spectra (Figure 2). The trans-geometry of 9-C double bond of 13 was deduced from the IR band at 975 cm$^{-1}$.

Analogous pair of methyl ethers, 15 and 16, were also isolated from a colored fraction. The isomer 15 exhibited a distinct optical rotation; $[\alpha]_D +1.8^\circ$. Although $[\alpha]_D$ value of another isomer 16 was zero, it showed plus optical rotation at shorter wave length.

Two quinones, 17 and 18, were obtained from less polar
fraction. The Rf values of the two quinones were quite identical under various solvent system, and the two compounds were only separable by preparative HPLC (MeOH : H₂O = 7 : 1). The mass (M⁺ m/e 440) and the ¹H-NMR (δ 2.01, 6H, quinone Me's) spectra of 18 revealed that this compound had one additional methyl group on the quinone nucleus of 17. The position of the methyl group was determined to be 5'-C, because the broad triplet at δ 6.44 due to the quinone proton collapsed into a sharp singlet on irradiation at δ 3.09 (1-methylene protons).

From the least polar fraction, 2-geranylgeranyl-6-methylbenzoquinone (19), which was named as sargaquinone, was isolated. Sargaquinone (19) is possibly a precursor of geranylgeranylbenzoquinone derivatives found in some Sargassum species.

As for the biosynthesis of the present diterpenoid-substituted benzoquinone derivatives, the following Scheme, involving the pentaene (A) and epoxide (B), is proposed.

\[ 19 \rightarrow \begin{array}{c}
\text{Ar} \\
\text{H}_2\text{O} \downarrow \\
\text{11} \text{ and } 13 \\
\begin{array}{c}
\text{15 and 16}
\end{array}
\end{array} \rightarrow \begin{array}{c}
\text{Ar} \\
\text{H}_2\text{O} \downarrow \\
\text{7} \\
\text{17} \rightarrow \text{20}
\end{array} \]
I-C  Components of Sargassum micranthum

Methanol extract of fresh S. micranthum was chromatographed on silica gel, affording three fractions, I-III. The fraction I consisted of almost pure farnesylacetone (21); IR(CCl₄) 1715 cm⁻¹; ¹H-NMR(CCl₄) δ 1.62 (9H, s), 1.68 (3H, s), 2.08 (3H, s), 5.08 (3H, brt), which was identified by converting into the semicarbazone; mp 79-80 °C (lit.8) mp 80.5-81.5 °C). Although the TLC of the fraction II showed only one spot, its HPLC exhibited five distinct peaks, and four new compounds (22-25) were obtained from this fraction by preparative HPLC (CH₃CN : H₂O = 3 : 1). The fraction III was a mixture of four compounds (27-30) which was separated by preparative TLC and HPLC.

The molecular formula, C₁₈H₃₀O₂ (M⁺ m/e 278.2230, calcd 278.2245), of compound 22 corresponded to that of dihydro-monooxofarnesylacetone. The presence of O=C-CH=C-CH₃ moiety and an acetyl group was deduced from the IR absorption bands at 1680 and 1715 cm⁻¹, the UV absorption maximum at 239 nm (ε 10500), and the ¹H-NMR signals at δ 1.85 (3H, d, J=1.5 Hz), 5.95 (1H, brs) and 2.07 (3H, s). The NMR spectrum also suggested the presence of isopropyl [δ 0.92 (6H, d, J=7 Hz)], vinyl methyl [δ 1.62 (3H, s)], and trisubstituted olefin [δ 5.10 (1H, brt, J=7 Hz)] groups. The stereochemistry of the double bonds at 5-C and 10-C was determined to be E and Z, respectively, from the chemical shifts of the methyl groups at
Figure 3.

<table>
<thead>
<tr>
<th>Fragment</th>
<th>Found</th>
<th>Calcd</th>
<th>Formula</th>
</tr>
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<tbody>
<tr>
<td>a</td>
<td>235.1667</td>
<td>.1698</td>
<td>C_{15}H_{23}O_2</td>
</tr>
<tr>
<td>b</td>
<td>221.1545</td>
<td>.1541</td>
<td>C_{14}H_{21}O_2</td>
</tr>
<tr>
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<td>.1592</td>
<td>C_{13}H_{21}O_2</td>
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<tr>
<td>d</td>
<td>140.1198</td>
<td>.1201</td>
<td>C_{9}H_{16}O</td>
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<tr>
<td>e</td>
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<td>.1279</td>
<td>C_{10}H_{17}O</td>
</tr>
<tr>
<td>f</td>
<td>125.0950</td>
<td>.0966</td>
<td>C_{6}H_{13}O</td>
</tr>
<tr>
<td>g</td>
<td>235.2029</td>
<td>.2061</td>
<td>C_{16}H_{27}O</td>
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6-C (δ 1.62) and 10-C (δ 1.85). The structure was further verified by high resolution mass spectrum as described in the Figure 3. Hydrogenation of 22 afforded the tetrahydro derivative (26), C₁₈H₃₄O₂; m/e 282 (M⁺), 267 (M⁺-CH₃), 225 (M⁺-C₄H₉, M⁺-CH₂COCH₃), 182 (M⁺-Me₂CHCH₂COCH₃); IR(CCl₄) 1715 cm⁻¹.

Compound 23, C₁₈H₃₂O₂; m/e 280.2378 (M⁺), 262 (M⁺-H₂O), 223 (M⁺-C₄H₉, M⁺-CH₂COCH₃) was a dihydro derivative of compound 22. The IR spectrum (1710 cm⁻¹) showed the absence of an α,β-unsaturated carbonyl group, and the ¹H-NMR spectrum revealed the presence of an acetyl (δ 2.05, 3H, s), isopropyl (δ 0.90, 6H, d, J=7 Hz), and secondary methyl (δ 0.87, 3H, d, J=7 Hz) groups, together with a trisubstituted olefin group (δ 5.02, 1H, m). The structure 23 was confirmed by converting it into the diketone (26) by hydrogenation.

Compound 24, C₁₈H₂₈O₂; m/e 276.2141 (M⁺) and 219 (M⁺-CH₂COCH₃), showed a strong absorption maximum at 246 nm(ε 20900) in its UV spectrum, and exhibited IR absorption bands due to α,β-unsaturated carbonyl system at 1670 and 1625 cm⁻¹. The molecular formula corresponded to that of dehydro derivative of compound 22, and the presence of an isopropylidene group instead of isopropyl group was confirmed by its ¹H-NMR spectrum; δ 1.62 (3H, s, 6-Me), 1.86 (3H, s, 14-Me, trans to C=O), 2.05 (3H, s, COCH₃), 2.11 (6H, d, J=1 Hz, 10-Me and 14-Me, cis to C=O), 5.02 (1H, t, J=7 Hz, 5-H), and 5.90 (2H, m, 11, 13-H). The E-configuration of the double bond at 10-C was obvious from the downfield chemical shift (δ 2.11) of the
methyl group at 10-C.

**Compound 25**, C$_{18}$H$_{28}$O$_2$, was an isomer of 24, and showed the following spectral properties; m/e 276.2042 (M$^+$), 261 (M$^+$-CH$_3$), 233 (M$^+$-COCH$_3$), 83 (Me$_2$C=CHCO); IR(CCl$_4$) 1715, 1685, 1615 cm$^{-1}$; $^1$H-NMR(CCl$_4$) δ 1.62 (6H, s), 1.87 (3H, s), 2.04 (6H, s), 2.93 (2H, s), 5.0-5.3 (2H, m), 6.01 (1H, s). The stereochemistry of the double bonds at 5-C and 9-C was determined to be E from the chemical shifts of the methyl signals.

The structures 27-30 were assigned for the remaining new compounds on the basis of the following spectral properties.

**Compound 27**, C$_{18}$H$_{34}$O$_2$; m/e 282.2561 (M$^+$), 264 (M$^+$-H$_2$O), 225 (M$^+$-C$_4$H$_9$), 85 (Me$_2$CHCH$_2$CO); IR(CCl$_4$) 3620, 1710, 1615 cm$^{-1}$; $^1$H-NMR(CCl$_4$) δ 0.87 (3H, d, J=7 Hz), 0.92 (6H, d, J=7 Hz), 1.13 (3H, d, J=7 Hz), 1.62 (3H, s), 3.70 (1H, m), 5.10 (1H, m).

**Compound 28**, C$_{18}$H$_{32}$O$_2$; m/e 280.2393 (M$^+$), 265 (M$^+$-CH$_3$), 223 (M$^+$-C$_4$H$_9$), 85 (Me$_2$CHCH$_2$CO); [α]$_D$ -3.75° (CHCl$_3$, c 0.53); $\lambda_{max}$(EtOH) 241 nm (ε 9500); IR(CCl$_4$) 3620, 1685, 1620, 1110, 1050 cm$^{-1}$; $^1$H-NMR(CCl$_4$) δ 0.92 (6H, d, J=7 Hz), 1.13 (3H, d, J=7 Hz), 1.61 (3H, s), 2.09 (3H, s), 3.70 (1H, sextet, J=7 Hz), 5.10 (1H, t, J=7 Hz), 5.94 (1H, s).

**Compound 29**, C$_{18}$H$_{32}$O$_2$; m/e 280.2360 (M$^+$), 262 (M$^+$-H$_2$O), 247 (262-CH$_3$), 237 (M$^+$-C$_3$H$_7$), 223 (M$^+$-C$_4$H$_9$), 85 (base, Me$_2$CHCH$_2$CO); [α]$_D$ -3.31° (CHCl$_3$, c 0.45); IR(CCl$_4$) 3620, 1710 cm$^{-1}$; $^1$H-NMR(CCl$_4$) δ 0.90 (6H, d, J=7 Hz), 1.12 (3H, d, J=7 Hz), 1.61 (6H, s), 2.93 (2H, s), 3.73 (1H, sextet, J=7 Hz), 5.16 (2H, m).
Compound 30, C$_{18}$H$_{32}$O$_2$; m/e 280.2383 ($M^+$), 262 ($M^+\text{-H}_2\text{O}$), 223 ($M^+\text{-C}_4\text{H}_9$), 85 ($\text{Me}_2\text{CHCH}_2\text{CO}$); $[\alpha]_D$ -3.16° (CHCl$_3$, c 0.25),
$\lambda_{\text{max}}$ (EtOH) 239 nm (ε 10600), IR(CCl$_4$) 3620, 1685, 1615, 1170, 1150 cm$^{-1}$; $^1$H-NMR (CCl$_4$) δ 0.92 (6H, d, J=7 Hz), 1.13 (3H, d, J=7 Hz), 1.64 (3H, s), 1.85 (3H, s), 3.68 (1H, sextet, J=7 Hz), 5.10 (1H, t), 5.90 (1H, s).

The farnesylacetone derivatives reported here are supposed to be norditerpenes, derived from geranylgeranylbenzoquinones such as sargaquinoic acid (1) by the oxidative cleavage of the C-C bonds pointed by the dotted lines.
I-D Components of *Sargassum fulvum*¹⁰

Methanol extract of *S. fulvum* (7 Kg, collected at Awakominato, Chiba) gave a fraction, whose \(^1\text{H-NMR}\) spectrum showed signals characteristic of terminal methylene protons. I was able to isolate the "terminal methylene compound", and found that the compound is a quite new glyceride bearing a methacrylic acid moiety.

The methanol extract was concentrated into an aqueous residue, which was successively extracted with hexane and ether. The ether extract was concentrated to give a brown oil (4.2 g). Column chromatography of this residue on silica gel with dichloromethane-methanol (9:1) yielded a fraction (2.8 g), the \(^1\text{H-NMR}\) spectrum of which showed a couple of broad singlets at δ 6.4 and 5.9 ascribable to the terminal methylene protons. Isolation of the "terminal methylene compound" was extremely difficult, because the more it was purified, the more sensitive to air and light it became. Purification by preparative TLC was fruitless, because the compound changed to an unknown compound on the TLC plate. Isolation and purification were successfully achieved by repeated flash chromatography (hexane:ethyl acetate = 2:3) to give an oily substance (200 mg), showing a single spot on TLC.

The IR spectrum of this substance, [α]₁₀ +2.5° (CHCl₃, c 0.1), showed the bands at 3600-2200, 1690 (conjugated CO₂H), 1730 (CO₂R), and 1620 (=CH₂) cm⁻¹. Its \(^1\text{H-NMR}\) spectrum (100
MHz, CDCl₃) exhibited a set of signals due to an unsaturated fatty acid moiety at δ 5.3 (brt, CH=CH), 2.80 (brs, C=C-CH₂-C=), 2.32 (t, CH₂CH₂-C=O), 2.00 (m, CH₂CH₂-C=O), 1.64 (m, CH₂ to C=O), 1.25 (brs, CH₂'s), 0.90 (deformed t, CH₃). Also it showed poorly resolved multiplets in the region of 4.3-3.5 ppm, the pattern of which closely resembled that appearing in the ¹H-NMR spectrum of glycerine-1-stearate except a singlet at δ 4.20. The signals of the terminal methylene protons appeared at δ 6.41 (brs) and 5.95 (brs). The chemical shifts and the shapes of these two signals were reminiscent of those of the terminal methylene protons of dimethyl itaconate (δ 6.31 and 5.70).

Detailed inspection of the 360 MHz ¹H-NMR spectrum (CDCl₃) revealed that the substance had the structure 31. All the

31: R₁ = H, R₂ = C₁ᵡH₃₁CO
   a: R₁ = H, R₂ = C₁ᵡH₃₅CO
   (fulvic acid)

32: R₁ = H, R₂ = H
33: R₁ = Ac, R₂ = C₁ᵡH₃₁/₃₅CO
protons belonging to the glycerine moiety formed the second-ordered coupling system \[ \delta 4.171 (2H, 7-H, ABX, J_{AB}=9.9 \text{ Hz}, J_{AX}=5.9 \text{ Hz}, J_{BX}=2.9 \text{ Hz}), 4.054 (1H, 6-H, ABX, pseudoquintet), 3.573 (2H, 5-H, ABX, J_{AB}=9.9 \text{ Hz}, J_{AX}=6.3 \text{ Hz}, J_{BX}=5.4 \text{ Hz}) \]. The methylene protons at 4-C appeared as a pair of doublets (J=1.2 Hz) at \( \delta 5.970 \) and 6.444, both of which were sharpened by irradiating the singlet at \( \delta 4.222 \) (2H, 3-H), establishing the allylic relationship of these two methylene groups.

Attempts to produce \( 32 \) by hydrolysis of \( 31 \) failed because of the fragility of the methacrylic acid moiety. Treatment of \( 31 \) with diazomethane gave a pyrazoline \( 34 \), \( ^1\text{H-NMR(CDCl}_3) \delta 3.67 \) (3H, s, COOCH\(_3\)), 4.47 (2H, t, J=8 Hz). Acetylation of \( 31 \) with acetic anhydride in pyridine gave rise to an acetate \( 33 \). IR(CHCl\(_3\)) 1735 and 1690 cm\(^{-1}\). Although this acetate showed a single spot on TLC after purification by column chromatography, two acetyl signals appeared in the \( ^1\text{H-NMR (360 MHz,CDCl}_3) \) spectrum; \( \delta 2.078, 2.080 \) (3H, COCH\(_3\)), 3.652 (2H, d, 5-H, J=5.4 Hz), 4.264 (2H, ABX, 7-H, J\(_{AB}=11.3 \) Hz, J\(_{AX}=5.9 \) Hz, J\(_{BX}=4.1 \) Hz), 5.22 (1H, pseudoquintet, 6-H), 5.961 (1H, d, 4-H, J=1.4 Hz), and 6.436 (1H, d, 4-H, J=1.4 Hz). This indicated that \( 31 \) was a mixture of \( 31a \) and \( 31b \). Separation of \( 31a \) and \( 31b \) was unsuccessful.

In order to verify the carbon skeleton of \( 31 \), the compound \( 38 \) was synthesized (Figure 4), and the \( ^{13}\text{C-NMR spectra of 33 and 38 were compared (Table 4): Etheration of the acetonide 35 with the bromide 36}^{11} \) and sodium hydride in dimethylformamide.

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Figure 4.

![Chemical structure diagram](image)

(Numbering is for convenience.)

Table 4. $^{13}$C-NMR chemical shifts of compounds 33 and 38.

<table>
<thead>
<tr>
<th></th>
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<th>38</th>
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<td>1-C</td>
<td>170.46</td>
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<td>136.41</td>
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<tr>
<td>3-C</td>
<td>69.28*</td>
<td>68.90**</td>
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<td>4-C</td>
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<td>6-C</td>
<td>70.42</td>
<td>70.17</td>
</tr>
<tr>
<td>7-C</td>
<td>69.37*</td>
<td>69.54**</td>
</tr>
</tbody>
</table>

*,** Chemical shifts are interchangeable.

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produced 37. The acetonide group of 37 was cleaved by acidic methanol, and the resulting diol was acetylated to give the diacetate 38. $^1$H-NMR (CDCl$_3$) δ 2.02 (3H, s, Ac), 2.08 (3H, s, Ac), 3.47 (2H, d, J=6 Hz, 5-H), 3.68 (3H, s, COOMe), 4.20 (2H, d, J=1 Hz, 3-H), 4.20 (2H, ABX, $J_{AB}$=12 Hz, $J_{AX}$=4 Hz, $J_{BX}$=6 Hz, 7-H), 5.18 (1H, quintet, 6-H), 5.86 (1H, splitted s, 4-H), 6.30 (1H, splitted s, 4-H). The chemical shifts of the carbons 1-7 of the diacetate were reasonably correspondent to those of 33, establishing the skeleton of 31. I named the compound 32, the basic component of 31, as fulvellic acid.

The high resolution mass spectrum of 31 showed a molecular peak of 31a at m/e 504.307 (C$_{29}$H$_{44}$O$_7$), and a fragment at m/e 448.317 (C$_{27}$H$_{44}$O$_5$), formed from 31b (C$_{29}$H$_{48}$O$_7$; m/e 508 in the low resolution MS) by loss of acetic acid. The composition of the fatty acid portion of 31 was confirmed by the following experiment: Treatment of 31 in benzene with a catalytic amount of methanolic m-trifluoromethylphenyltrimethylammonium hydroxide$^{12}$ afforded a mixture of methyl esters. GC-MS analysis of this mixture revealed that it consisted of mainly two esters (90 % of the ester fraction), C$_{15}$H$_{31}$COOCH$_3$ (m/e 318) and C$_{19}$H$_{35}$COOCH$_3$ (m/e 322) (3:1), which were derived from 31a and 31b, respectively.

Among the Sargassum algae that I investigated, sagamianum, ringgoldianum, piluliferum, giganteifolium, yendoi, and hemiphyllum, were found to contain this new type of glyceride, although Hizikia fusiforme, which was taxonomically close to
Sargassum algae, did not produce the glyceride 31. Chemo-
taxonomical and biological significance of this "unusual fat" is of interest.
EXPERIMENTAL

Infrared spectra were recorded on a HITACHI 215 spectrophotometer and ultraviolet spectra were recorded on a HITACHI 340 spectrophotometer. Optical rotations were recorded on a JASCO DIP-181 polarimeter, using a 10-cm microcell. $^1H$-NMR spectra were recorded on JEOL JNM-MH-100, HITACHI R24, and HITACHI R20 NMR spectrometers; chemical shifts are reported relative to Me$_4$Si(δ0), and coupling constants are given in hertz. Low-resolution mass spectra were obtained from a HITACHI RMU-6M mass spectrometer.

Algal collection, extraction, and isolation of compounds. Algae were collected at Awakominato, Chiba, in spring from 1978 to 1980. The fresh algae were soaked in MeOH immediately after the collection and allowed to stand for 1 week. The MeOH was decanted, and the residual material was again extracted with fresh MeOH for 1 week. The combined MeOH extracts were concentrated on a rotary evaporator, and the residue was successively washed with hexane, ether, and ethyl acetate. Each extract was concentrated, and the residue was fractionally separated by chromatography on silica gel (Merck, Kieselgel 60), and further purified by preparative TLC (Merck, Kieselgel 60, GF$_{254}$) and HPLC (LS-410K).

Acetylations. All acetylations were conducted in a
similar fashion. Acetic anhydride was added to a solution of
the natural product in pyridine, and the reaction mixture was
allowed to stand at room temperature overnight. The excess
reagents were then removed in vacuo to yield the acetylated
products, which were purified, when necessary, by preparative
TLC.

Sargaquinial (2). MS m/e 408(M⁺), 393, 390, 379, 365,
177, 175(base), 137, 69; ¹H-NMR(100 MHz, CDCl₃) δ 1.50(3H,s),
1.58(9H,s), 2.00(3H,s), 3.15(2H,d,J=7 Hz), 5.20(3H,m),
6.5(3H,m), 9.36(1H,s).

Reductive acetylation of sargaquinoic acid (1) to 3. A
solution of 1 (511 mg) and zinc (500 mg) in 5 ml of acetic
anhydride and triethylamine (3 drops) was stirred for 10 min.
The reaction was quenched by the addition of water, and the
aqueous phase was extracted with ether. The ether layer was
everaged, and the residue was chromatographed on silica-gel
column to give the diacetate 3: C₃₁H₄₂O₆, MS m/e 510(M⁺), 492,
450, 441, 423, 408, 289, 271, 217(base), 192, 69; IR(CHCl₃)
3300-2300, 1750, 1680 cm⁻¹; ¹H-NMR(100 MHz,CDCl₃) δ
1.60(6H,bs), 1.68(6H,bs), 2.13, 2.24, 2.29(each 3H,s),
3.20(2H,d,J=8 Hz), 5.1(3H,m), 6.01(1H,t,J=7 Hz), 6.82(2H,bs).

Reduction of 3 to 4. To a solution of 3 (200 mg) in
ether (20 ml) was added an excess amount of LiAlH₄. The

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reaction mixture was refluxed for 3 hr, and quenched by careful dropwise addition of H₂O. The mixture was partitioned between ether and H₂O, and the ether layer was evaporated to give the triol (95 mg). The triol was allowed to stand at r.t. overnight to yield the quinone 4: C₂₇H₃₈O₃, IR(CHCl₃) 1645, 1610 cm⁻¹; ¹H-NMR(60 MHz,CDCl₃) δ 1.60(9H,bs), 1.65(3H,bs), 2.05(3H,bs), 3.05(2H, bd, J=7 Hz), 4.07(2H, bs), 4.9-5.3(4H,m), 6.45(2H,m).

Oxidation of 4 to 5. A solution of 4 (9.7 mg) in CH₂Cl₂ (1 ml) was added to 1 equivalent of pyridinium chlorochromate. After 5 min, the reaction was quenched by the addition of EtOH, and the mixture was partitioned between ether and H₂O. The ether layer was concentrated in vacuo, and purified by preparative TLC, giving 5: C₂₇H₃₆O₃. The mass spectrum is almost identical with that of sargaquinal (2); IR(CHCl₃) 1650, 1610, 910 cm⁻¹; ¹H-NMR(100 MHz,CDCl₃) δ 1.58, 1.63(each 6H,bs), 2.07(3H,bs), 3.13(2H, bd, J=7 Hz), 5.1(3H,m), 6.5(3H,m), 10.11(1H,s).

Degradation of sargatetraol (7) to aldehydes 9 and 10. A saturated solution (5 ml) of H₅IO₆ in ether was added to 7 (34.7 mg), and the solution was stirred at r.t. for 10 min. The mixture was diluted with water and extracted with ether. The ether layer was dried over MgSO₄ and concentrated in vacuo. Purification by preparative TLC yielded the quinone 9 (9.6 mg).
and geranial (7.0 mg).

**Oxidation of sargatetraol (7) to 17.** A solution of 7 (58 mg) in ether was treated with anhydrous sodium acetate (273 mg), to absorb the water formed, and the dry silver oxide was added with shaking until there was no further deepening in color. After stirring for 40 min at r.t., the reaction mixture was filtered to remove silver, and the filtrate was evaporated to give 17 (50.6 mg).

**Conversion of 17 to 20.** A solution of 17 (41.9 mg) in pyridine (1 ml) was heated at 50 °C for 21 hr. Then the excess pyridine was removed in vacuo, and the residue was purified by preparative TLC to give 20 (12.4 mg): C_{27}H_{38}O_{4}, ^1H-NMR (60 MHz, CDCl₃) δ 1.33 (3H, s), 1.58, 1.65 (each 6H, bs), 2.12 (3H, bs), 3.82 (1H, d, J=8 Hz), 4.32 (1H, t, J=8.5 Hz), 5.2 (3H, m), 5.55, 6.27 (each 1H, d, J=10 Hz), 6.34, 6.50 (each 1H, d, J=2.5 Hz).

**Hydrogenation of 22 and 23 to 26.** Compound 22 (and 23) was dissolved in EtOH, and stirred overnight with 10% Pd/C in a H₂ atmosphere. The reaction mixture was filtered and concentrated to give the perhydro compound 26.

**Methylation of 31 to 34.** 31 (34 mg) was treated with a solution of excess diazomethane in ether. After 5 min, the solution was concentrated to afford an oil (35 mg): ^1H-NMR (100
MHz, CCl₄) δ 3.47(2H, d, J=5 Hz, 5-H), 3.70(3H, s, OCH₃), 3.9-4.1(4H, m, 3, 7-H), 4.52(2H, t, J=8 Hz, N-CH₂), 4.96(1H, m, 6-H), 5.25(m, olefinic H).

Preparation of 37. To a solution of the alcohol 35 (1.292 g) in dry DMF (20 ml) was added sodium hydride (428 mg; as a 60% dispersion in a mineral oil) during 30 min, and the mixture was stirred at r.t. for 1 hr. A solution of the bromide 36 (1.836 g) in DMF (4 ml) was added via syringe during 10 min (exothermic reaction), and the mixture was stirred at r.t. overnight. Water was added, and the product was extracted with ether. The ether layer was washed with water and brine, and dried over Na₂SO₄. Purification by flash chromatography afforded almost pure 37 (153 mg): C₁₁H₁₈O₅, ¹H-NMR(100 MHz, CDCl₃) δ 1.34, 1.39(each 3H, s), 3.54(2H, d, J=5 Hz, 5-H), 3.74(3H, s, OCH₃), 3.7(1H, m, 6-H), 4.1(2H, m, 7-H), 4.20(2H, bs, 3-H), 5.84, 6.24(each 1H, bs, 4-H).

Conversion of 37 to 38. A solution of the acetonide 37 (20.3 mg) in methanol (0.15 ml) was treated with a small piece of crystals of p-TsOH. After 22 hr, the reaction mixture was diluted with MeOH, a drop of pyridine was added, and the solvent was evaporated. To the colorless residue, pyridine (0.2 ml) and acetic anhydride (0.2 ml) were added, and the resulting mixture was allowed to stand at r.t. for 5 hr. The mixture was concentrated using an oil pump at r.t., giving rise
to an oil.

**Methanolysis of 31.** To a solution of 31 (12 mg) in benzene (0.5 ml) was added a 5% MeOH solution of m-trifluoromethylphenyltrimethylammonium hydroxide (0.2 ml). The solution was allowed to stand at r.t. for 1.5 hr. The reaction mixture was chromatographed on silica gel with CH$_2$Cl$_2$, affording an oil (9 mg). GC-MS of this oil was measured.
REFERENCES

12) D. K. McCreary, W. C. Kossa, S. Ramachandran, and R. R.
CHAPTER II

STUDIES ON METABOLITES OF THE DICTYOTACEAE
BROWN ALGAE
The typical metabolites of the Dictyotaceae brown algae thus far reported are cyclic diterpenes. They often have a familiar sesquiterpene ring system with an additional isoprene unit in the side-chain. For example, the carbon skeleton of pachydictyol A (12) is an 'extended' guiane sesquiterpene. There are, however, some very interesting exceptions to that observation.

In this chapter the diterpenes from the Dictyotaceae are organized according to the kinds of carbocyclic rings in order of the biogenesis pathways (II-G).
II-A  Diterpenes with a Cyclodecane Skeleton

Natural products possessing a cyclodecane framework are frequently found as germacrane sesquiterpenoids in terrestrial plants.2) On the contrary, diterpenoids having a ten-membered ring are much rarer, and it is only ten years ago that the first germacrane-type diterpene, dilloh (1),3) was isolated from an alga. Since then, several other diterpenoids having a ten-membered ring have been obtained from marine resources.4-6) In the course of my study on the constituents of the brown alga, Pachydictyon coriaceum, I have isolated three new germacrane-type diterpenes together with known diterpenes, 3-acetoxyacetyldilohol (2)4) and obscuronatin (3).5) I would describe the structural elucidation of the new compounds, as well as the conformational analysis of these compounds.

\[ \begin{align*}
\text{1: } & X=H, R=H \\
\text{2: } & X=OAc, R=Ac
\end{align*} \]

3-Hydroxyacetyldilohol (4),7) \( \text{C}_{22}\text{H}_{36}\text{O}_3 \), [\( \alpha \)]\( \text{D} \) -7.2° (c 0.64, CHCl\( _3 \)), IR(CHCl\( _3 \)) 3600, 1730, 1240 cm\(^{-1}\), MS m/e 348(M\(^+\)), 306, 288, 270, 177, 159, 109, 69(base), exhibited the \( ^1\text{H-NMR} \) spectrum very similar with that of 3-acetoxyacetyldilohol
Noticeable differences were that (1) only one acetyl signal was found in 4 and (2) the chemical shift of 3-H in 2 (δ 5.0) moved up to δ 4.36 (t, J = 3 Hz) in 4. On the basis of these properties, the structure 4 was assigned for 3-hydroxy-acetyldilophol, and the structure was confirmed by conversion of 4 into 2 by acetylation.

\[
\begin{align*}
4 & : X = \text{OH}, R = \text{Ac} \\
5 & : X = \text{H}, R = \text{Ac}
\end{align*}
\]

From a less polar fraction, dilophol acetate (5), \([\alpha]_D -30.9^\circ\) (c 0.57, CHCl\(_3\)), IR(CHCl\(_3\)) 1730, 1240 cm\(^{-1}\), was isolated. Hydrolysis (KOH/MeOH) of dilophol acetate produced dilophol (1), \([\alpha]_D -26.1^\circ\) (c 0.44, CHCl\(_3\)). It is noteworthy that dilophol acetate changed into a compound on standing with silica gel in CH\(_2\)Cl\(_2\) at room temperature for 24 hr. The product was characterized as obscuronatin (3), \([\alpha]_D -112^\circ\) (c 0.49, CHCl\(_3\)), by comparison of the spectral properties. The relative stereochemistry of obscuronatin has been recently confirmed by synthesis, and since the absolute configuration of dilophol (1) has been established, the absolute configuration of obscuronatin in the present alga was determined as in 3 by the above transformation. The 400 MHz \(^1\)H-NMR spectrum (27
°C) of 3 reveals the well-defined signals. Also the $^{13}$C-NMR spectrum (22.5 MHz at 27 °C) exhibited sharp signals. These indicate that obscuronatone takes one stable conformation in contrast with other germacrene-type diterpenes. The conformation of obscuronatone was determined as depicted in 6 by analysis of the spin coupling patterns of the key protons (1-H, 2-H, 5-H, 6-H) and observation of NOEs between the protons as shown in 6. Experiments using a paramagnetic shift reagent [Eu(fod)$_3$] also supported the conformation 6.

Formation of obscuronatone (3) from dilophol acetate (5) is reasonably interpreted by (i) intramolecular [1,5] shift of the acetoxy group to 4-C followed by hydrolysis, or (ii) attack of water to 4-C with concomitant removal of the acetoxy group.

Acetoxypachydiol (7), $^{7}$C$_{22}$H$_{36}$O$_4$ (m/e for M$^+$, 364.248), $[\alpha]_D$ -76.4 ° (c 0.55, CHCl$_3$), was obtained as a colorless oil. The IR spectrum (CCl$_4$) implies the presence of acetoxy (1750 and 1240 cm$^{-1}$) and hydroxy (3300-3600 cm$^{-1}$) groups. On
acetylation (Ac₂O/py), two acetyl groups were incorporated (¹H-NMR), indicating that two hydroxy groups were present. Fragments at m/e 109 and 69, and the ¹H-NMR signals depicted in the partial structure suggest the existence of the side chain A. Decoupling works (400 MHz; -50 °C) inferred additional partial structures B and C. The downfield (δ 6.10) chemical shift of the olefin proton in moiety B indicates the cis relationship between this olefin proton and the acetoxyethyl group. Other three carbons and five protons which are not discussed above must be two CH₂'s and one CH, because all of five methyl groups that exist in acetoxybachydiol (¹H and ¹³C-NMR) are found in A to C. Consideration of these facts and biogenesis of diterpenes led to the gross structure 7 (without stereochemistry) or its isomer in which the glycol moiety is located on 8-C and 9-C. In the 400 MHz ¹H-NMR spectrum measured at 27 °C, several protons appear as broad signals, indicating that acetoxybachydiol takes two or more conformations, which invert in a moderate rate on an NMR time scale. Interestingly, when the spectrum was taken at -50 °C, only one
$J$ values (-50°C) of protons

$J$ 2α- 2α = 13.0 Hz
$J$ 2α- 1 = 0 Hz
$J$ 2β- 1 = 11.4 Hz
$J$ 2α- 3 = 9.2 Hz
$J$ 2β- 3 = 4.8 Hz
$J_{20α-20β} = 12.1$ Hz
$J$ 5 - 6 = 9.9 Hz
$J$ 6 - 7 = 0 Hz

---

Fig. 1 $^{13}$C-NMR spectra (100 MHz; CD$_2$Cl$_2$) of acetoxypachydiol (7).
set of signals were observed. Similar phenomena were observed in the $^{13}$C-NMR spectra; while the spectrum measured at 27 °C (100 MHz) showed several broad signals (Figure 1) and the number of carbon signals was less than the one expected from the molecular formula, the spectrum recorded at -50 °C (Figure 1) exhibited 22 sharp signals. These facts suggest that acetoxypaclydiol takes a major (possibly >98%) conformation at -50 °C, and the minor conformer(s), whose population increases as the temperature rises, is not observable in the NMR spectra at that low temperature. Double resonance experiments (400 MHz) performed at -50 °C provided the spin coupling constants of the protons (see structure 7). The coupling constants are interpretable only when the conformation and relative configurations of the substituents are supposed as seen in 9 or 10. In order to differentiate the two, NOE experiments were carried

\[\text{AcO} \quad \text{Me} \quad \text{H} \quad \text{NOE} \]

\[(10: 8\beta, 9\alpha - \text{diol instead of } 5,6-\text{diol})\]
out at -50 °C using a 400 MHz spectrometer, but, unexpectedly, no NOE was observed between any pairs of protons by this high field spectrometer. On the other hand, when a 250 MHz instrument was used, small but distinct NOEs between several pairs of protons were observed. These findings (depicted in 9) confirmed the structure and stereochemistry of acetoxyphachydiol to be 9. MM2 calculation revealed that free energy difference between 9 and the next favorable conformation 11 was ca. 1 Kcal. The dibenzoate 8 exhibited negative splitted Cotton effects (λ<sub>ext</sub> 237 nm, Δ ε -9.8; λ<sub>ext</sub> 222 nm, Δ ε +9.8), and, hence, the absolute configuration of acetoxyphachydiol was determined as depicted in 9.10)

Acetoxyphachydiol (7) is the first example of diterpene that possesses a 1,4-cyclodecadiene skeleton.
II-B  Diterpenes with a Perhydroazulene Skeleton

Species of brown algae belonging to the family Dictyotaceae have been a rich source of diterpenoids containing the perhydroazulene ring system. Pachydictyol A (12),\(^1\) which was isolated by Hirschfeld et al. from \textit{P. coriaceum} at California was the first member of this family to be reported. Subsequently a number of oxygenated derivatives of pachydictyol A have been described.

In this section, I would like to describe the diterpenoid constituents having a perhydroazulene skeleton isolated from Dictyotaceae brown algae.

\[ \text{Diagram Images} \]
Methanol extract of *P. coriaceum* afforded three new diterpenes, acetylpidictyl C (16),\(^{11}\) isopachydictyl A (18), and hydroxydictyoxide (19), having a perhydroazulene skeleton, together with the known diterpenes, pachydictyl A (12),\(^{1}\) dictyl C (13),\(^{12}\) dictyl E (14),\(^{12}\) and dictyoxide (15).\(^{13}\)

**Acetylpidictyl C** (16; 0.1 % of the methanol extract), oil, [\(\alpha\)]\(_D\) -3.6 ° (c 0.6, CHCl\(_3\)), unexpectedly resisted acetylation (Ac\(_2\)O/Py at room temperature), although a secondary hydroxy group was obviously present (\(^1\)H-NMR; \(\delta\) 3.85). Acetylation at higher temperature (100 °C/48 hr) gave diacetate (17). This inertness of the hydroxy group of 16 was reminiscent of the sterically hindered C-6 hydroxy group of dictyl C (13). Indeed, hydrolysis of 16 (KOH/MeOH/3 hr) at 65 °C yielded 13, which was identified by comparison of its \(^1\)H and \(^13\)C-NMR spectra with those reported for dictyl C.\(^{12}\)

\[
\begin{align*}
\text{Ac}_2\text{O/Py} & \quad \text{Acetate (17)} \\
100^\circ\text{C} & \quad \text{dictyl C (13)} \\
\text{OH}^- &
\end{align*}
\]

**Isopachydictyl A** (18), oil, [\(\alpha\)]\(_D\) -3.6 ° (c 0.6, CHCl\(_3\)), was separable by HPLC (MeOH : H\(_2\)O = 9 : 1) from the fraction
containing pachydictyol A (12), and found to be an isomer of pachydictyol A by MS. $^1$H-NMR spectrum (CDCl$_3$) resembles that of pachydictyol A, except for the signals of an olefinic proton (δ 5.47) and an olefinic methyl (δ 1.67) instead of the exomethylene signals in 12. From these data, structure 18 was deduced for isopachydictyol A, and confirmed by comparison of its spectra with those reported for the derivative of dictyol B.14)

![Chemical Structure](image)

**Hydroxydictyoxide (19), C$_{20}$H$_{32}$O$_4$, MS m/e 304 (M$^+$), 286, 268, 109 showed the IR band at 3610 cm$^{-1}$ assignable to a hydroxy group. The $^1$H-NMR spectrum of this compound is very similar with that of dictyoxide (15).13) Noticeable difference was that the signal of an oxygen-bearing methine proton (δ 4.48) appeared in 19. Decoupling works revealed that this proton was coupled with the olefinic proton (δ 5.67, J = 2.5 Hz) and the methine proton (δ 2.34, J = 4 Hz). This spectral property allowed me to deduce the structure 19 for hydroxy-
dictyoxide. The relative configuration of the hydroxy group at 2-C was determined as depicted in structure 19 by the coupling constant between 1-H and 2-H (4 Hz), and the observation of NOE between these protons.
II-C Diterpenes with a Xenicane Skeleton

Natural products having a cyclononane skeleton are one of the most infrequent groups of compounds, and since the structure of caryophyllene,\textsuperscript{15} the first example of this category, was reported, a lot of synthetic chemists have been involved in the synthesis of the compound and its analogues because of its unique carbon framework. However, not so many compounds possessing a cyclononane skeleton have been reported so far. Very recently, xenicin (20) was isolated from a soft coral, \textit{Xenia elongata}.\textsuperscript{16} Xenicin is the first diterpenoid with a cyclononane skeleton and its framework has been conventionally called as a xenicane skeleton after its name.

\[
\begin{align*}
\text{AcO} & \quad \text{AcO} \\
\text{OAc} & \quad \text{OAc} \\
\text{H} & \quad \text{H} \\
\text{OAc} & \\
\text{AcO} & \\
\end{align*}
\]

I was able to isolate a number of xenicane type compounds from the Dictyotaceae seaweeds, several of which were found to have unique structures quite different from that of xenicin (20).

Chromatographic separation of the methanol extract of \textit{P. coriaceum} afforded several new compounds having a xenicane
skeleton, together with the known diterpenes, dictyodial (21),\textsuperscript{17} dictyolactone (22),\textsuperscript{17} and isodictyohemiacetal (23).\textsuperscript{18}

Acetyldictyonal (24, 0.1 % of the methanol extract)\textsuperscript{11} exhibited IR bands due to an \( \alpha,\beta \)-unsaturated aldehyde (2720 and 1685 cm\(^{-1}\)) and an ester (1735 cm\(^{-1}\)) groups. The structure 24 was deduced for acetyldictyonal from the spectral data. In the \( ^1\)H-NMR spectrum, the proton at 2-C appeared as a broad triplet (\( \delta 2.76, J = 8 \) Hz). Decoupling works revealed that this proton was also coupled with the aldehyde proton (\( \delta 9.40, J = 1.0 \) Hz), but not with the vicinal proton at 3-C. On the analogy of the corresponding protons of dictyodial (21), the configurations at 2-C and 3-C were deduced as illustrated in the structure 24.
The structure was unambiguously determined by the chemical conversion; hydrolysis (Na₂CO₃/MeOH) of 24 gave the hemiacetal (25) as an epimeric mixture, which was oxidized with manganese dioxide, affording dictyolactone (22).

Acetals (26a, 0.2 %, and 26b; 0.2 %) were separable by column chromatography. Each of them showed two methoxy signals, besides two 1H-singlets due to acetal protons (18 and 19-H) in its ¹H-NMR spectrum. The configuration at 18-C of each isomer was deduced by the null coupling constant between 2 and 18-H, although the configuration at 19-C was not clarified.
When the acetals were allowed to stand with silica gel, they changed into dictyodial (21), together with sanadaol (56). These acetals can be artifacts, which was formed from dictyodial (21) and methanol.

**Neodictyolactone (27),**<sup>20</sup> C<sub>20</sub>H<sub>30</sub>O<sub>2</sub>, [α]<sub>D</sub> -43.4° (c 0.29, CHCl<sub>3</sub>), shows IR bands at 1750 (s) and 1645 (w) cm<sup>-1</sup> attributable to an α,β-unsaturated γ-lactone moiety, the presence of which was confirmed by the UV maximum at 220 nm (ε 7800) and a <sup>1</sup>H-NMR (90 MHz) signal at δ 4.56 (2H, s) ascribable to the methylene protons at the γ-position. From the MS fragments at m/e 109 and 191 (See the structure 27.) together with the <sup>13</sup>C-NMR spectrum, it is obvious that 6-methyl-5-hepten-2-yl group, a side chain, is included in this compound. The <sup>13</sup>C-NMR spectrum reveals the presence of another trisubstituted olefin bearing a methyl group [δ 15.8 (q; 20-C), 123.5 (d; 7-C), 140.0 (s; 6-C)], and also four methylene and one methine groups in addition to the aforementioned moieties, which indicates that one more ring other than the lactone ring is included in
neodictyolactone. The configuration of the trisubstituted olefin is deduced to be E from the chemical shift (δ 15.8) of the olefinic methyl. In the $^1$H-NMR spectrum, this methyl group appears as a broad singlet at δ 1.26. This highly shielded olefinic methyl is reminiscent of acetylcoriacenone (45), in which the olefinic methyl is shielded by a transannular effect of the cyclobutene group. These facts together with biogenetic considerations allowed me to propose two possible structures 27 and 28 for neodictyolactone. The position of the lactonic carbonyl, 18-C (27) or 19-C (28), was determined by the following chemical transformations (Figure 2). Neodictyo-

Figure 2.

![Chemical Structures](image-url)
lactone was reduced with lithium aluminum hydride to afford the diol 29 \( \delta 4.11 (2H, ABq, J = 11 \text{ Hz}), 4.12 (2H, s) \). The diol was treated with PCC in dichloromethane, giving rise to a lactone together with dictyofuran T (30),\(^{22}\) the formation of which supported the carbon framework of neodictyolactone. In this oxidation process, it is likely that the less hindered hydroxy group (19-C) of the diol 29 would have been oxidized in preference to the more hindered one (18-C),\(^{23}\) so that the resulting lactone would have the 19-keto structure (28). This lactone was different from neodictyolactone in TLC, GC, and MS, therefore, the structure 27 is assignable to neodictyolactone. NOEDS experiments (400 MHz) are consistent with the structure 27; on irradiation at \( \delta 4.60 (19-H_b) \), significant NOEs were detected for the signals of 9-H\(_b\) (\( \delta 2.3 \)) and 20-Me (\( \delta 1.26 \)).

18-Acetoxydictyolactone (31),\(^{20}\) has the molecular formula C\(_{22}\)H\(_{32}\)O\(_4\), suggesting that an acetoxy group is present in addition to a diterpenoid framework. The UV maximum at 224 nm (\( \epsilon 8200 \)), the IR bands at 1785 and 1640 cm\(^{-1} \), and the \(^1\)H-NMR signal at \( \delta 7.06 \) due to an olefinic proton are suggestive of an \( \alpha \)-alkyliedene-\( \gamma \)-lactone structure. This proton (9-H) was deduced to be adjacent to a doubly allylic methylene protons (8-H\(_2\); \( \delta 2.8-3.4 \)) as in dictyolactone (22),\(^{17}\) because irradiation of the latter affected the signals at \( \delta 7.06 \) (9-H) and also at 5.37 (7-H). The acetoxy group has to be located at 18-C, since the signal of the methine proton on the carbon bearing the acetoxy group shifts down to \( \delta 6.68 \). These findings
allowed me to deduce the structure of this compound to be $31$, and the other spectral properties are compatible with the structure. The relative configurations at 2, 3, and 18-C of $31$ were assigned as illustrated in the structure from the consideration of the null coupling constants between 18-H and 2-H, as well as 2-H and 3-H. Molecular models reveal that the dihedral angles formed by each of these protons are $90^\circ$ in $31$.

4-Acetoxycycloexolactone ($32$), $C_{22}H_{32}O_4$, $[\alpha]_D^{22} -224^\circ$ (c 0.86, CHCl$_3$), UV (EtOH) 220 nm (ε 8500), IR (CCl$_4$) 1760, 1740, 1640 cm$^{-1}$, is an isomer of acetoxycycloexolactone ($31$). The $^1H$-NMR spectrum of this compound is very similar with that of cycloexolactone ($22$)$^{17}$ except for the signals of an acetoxyl group ($\delta$ 2.03) and oxygen-bearing methine proton ($\delta$ 5.27). On the basis of the COSY spectrum, the acetoxyl group was deduced to be located at 4-C, and the relative configuration of this carbon was assigned as illustrated in the structure $32$ from the coupling constants ($J = 4.5, 2.3$ Hz) of this methine proton. The relative configurations of other carbons in this compound were
determined to be identical with those of dictyolactone (22) by comparison of the coupling pattern.

In the similar way as described for neodictyolactone, 18-acetoxydictyolactone and 4-acetoxydictyolactone, the structure of another new diterpene, isodictyoacetel,\textsuperscript{20} \([\alpha]_D^\text{D}
-7.7^\circ\text{ (c 0.75, CHCl}_3\), was elucidated to be 33. On hydrolysis of 33 (TsOH in dioxane-water) there was obtained a hemiacetal, which exhibits an acetalic methine proton signal at \(\delta 5.65\) in the \(^1\text{H}-\text{NMR}\) spectrum. This chemical shift and also other spectral features of this product are identical with those

\[33: R = \text{O}Me\] \[23: R = \text{OH}\]
reported for isodicyohemiacetal \(^{18}\). As observed in 18-acetoxydictyolactone \(^{31}\), the coupling constants, \(J_{2-3}\) and \(J_{2-18}\), in the \(^1\)H-NMR spectrum of \(^{33}\) are zero, which led to the assignment of the relative configurations at 2, 3, and 18-C as seen in the structure.

Further fractionation of the methanol extract afforded another new diterpene, \textbf{pachyaldehyde [(34); 3 mg]},\(^{24}\) composed of nineteen carbon atoms.

The proton-noise decoupled \(^{13}\)C-NMR spectrum of pachyaldehyde \((34)\), \([\alpha]_D -40^\circ \text{ (c 0.21, CHCl}_3\text{)},\) contains nineteen signals. The multiplicities of the carbon signals (off-resonance spectrum), which indicate the number of the protons, and the molecular ion at m/e 274 in the mass spectrum suggest the molecular formula \(C_{19}H_{30}O\) for pachyaldehyde. The high resolution mass spectrum supports this formula \((M^+, \text{m/e 274.229, } C_{19}H_{30}O \text{ requires 274.230})\). The \(^{13}\)C-NMR spectrum contains signals due to six olefinic carbon atoms (three C=C's) and an aldehydic carbon atom \((\delta 195.9)\), which show that pachyaldehyde is monocyclic. The presence of an \(\alpha,\beta\)-unsaturated aldehyde moiety was shown by the IR bands at 2720, 1685 (CHO), and 1610 (C=C) cm\(^{-1}\), and the \(^1\)H-NMR (90 MHz) signals at \(\delta 9.32\) (CHO) and 6.69 (H-C=C-CHO). The proton at \(\delta 6.69\) (9-H, dd, \(J = 8, 3 \text{ Hz}\)) is coupled with the methylene protons appearing at \(\delta 3.23\) (8-H\(_b\), ddd, \(J = 16, 12, 3 \text{ Hz}\)) and 2.96 (8-H\(_a\), ddd, \(J = 16, 8, 4 \text{ Hz}\)). The methylene protons are further coupled with the olefinic proton at \(\delta 5.39\) (7-H, dd, \(J = 12, 4 \text{ Hz}\)), irradiation
Table 1. The $^{13}$C n.m.r. data\textsuperscript{a} for pachyaldehyde (34), acetyl-dictyodal (24), dictyodial (21), and dictyolactone (22).

<table>
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<th>C atom</th>
<th>Pachyaldehyde (34)</th>
<th>Acetyl-dictyodal (24)</th>
<th>Dictyodial (21)</th>
<th>Dictyolactone (22)</th>
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\textsuperscript{a}Chemical shifts are relative to the center line of CDCl\textsubscript{3}.
\textsuperscript{b}Assignment may be reversed. \textsuperscript{c}Assignment of these signals appearing in the reference 17 should be corrected as in this Table.
Table 2. $^1$H N.m.r (400 MHz) data for pachyaldehyde (34).

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<td>10</td>
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<td>1.20 (m)</td>
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<td>19</td>
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<td>1.75 (br. s)</td>
</tr>
</tbody>
</table>

$^a$In CDCl$_3$ at 28° and from TMS as an internal standard.

$^J$(H-H) values in Hz: (2a-2b) 14, (2a-3) 7, (2b-3) 0, (4a-4b) 12, (4b-3) 12, (4a-5a) 5, (4a-5b) 3, (4b-5a) 12, (4b-5b) 4, (5a-5b) 12, (7-8a) 4, (7-8b) 12, (8a-8b) 16, (8a-9) 8, (8b-9) 3, (13-12) 7, (17-10) 7; others not resolved.
of which resulted in sharpening of the methyl signal at δ 1.75 (19-Me, bs). These data indicated the partial structure (OHC-\[C=CH-CH_2-CH=C=O-Me\]).

The presence of the 6-methyl-5-hepten-2-yl group, the side chain which is frequently encountered in the diterpenes isolated from the Dictyotaceae algae, was evident from the mass fragment at m/e 109, and also the $^{13}$C-NMR signals which correspond well with the side chain carbon atoms (see structure 34 and Table 1). The $^{13}$C-NMR spectrum shows the presence of three additional methylene and one methine groups. Biogenetic considerations led to the structure 34 (or its alternative having the side chain at 4-C) for pachyaldehyde. The configuration of the double bond at 1(9)-C was deduced as E from the upfield chemical shift of the aldehyde proton (δ 9.32) in the $^1$H-NMR spectrum. Also, the E-configuration of C$_6$=C$_7$ was determined from the $^{13}$C-NMR chemical shift of the 19-methyl group (δ 17.6).

As to the position of the side chain, 3-C was considered to be more appropriate than 4-C, because the $^{13}$C-NMR spectrum of pachyaldehyde (34) corresponds well with those of acetyl-dictyolal (24), dictyodial (21), and dictyolactone (22), as shown in Table 1. Furthermore, the 400 MHz $^1$H-NMR spectrum (Table 2) of pachyaldehyde established the coupling constants between the protons on the ring carbon atoms, providing the conformation of the cyclononadiene ring illustrated in 35, and also further suggesting the position of
the side chain at 3-C. The NOE found for 34 (depicted in 35 by arrows) are consistent with the proposed conformation.

Pachyaldehyde is the first example of a norditerpene possessing a cyclononadiene skeleton.

Fractionation of the methanol extract of Dictyota dichotoma afforded a novel new diterpenoid, dictyotalide B, which has a bridged γ-lactone ring having a double bond at bridgehead.

Dictyotalide B (36), C_{22}H_{32}O_{4} (m/e 360.2338), [α]_D ^{+} +50.3° (c 0.59, CHCl_{3}), is an isomer of 4-acetoxydictyolactone (32). The presence of a γ-lactone, 6-methyl-5-hepten-2-yl group, and a trisubstituted olefin moiety bearing a methyl group is apparent from the spectral properties (Table 3). The absence of the downfield olefinic proton observed for 9-H of 32 strongly suggested that dictyotalide B had the structure 37 or its 18-C
carbonyl isomer 38, in which the C9(C1) double bond of 32 migrated to C1(C2). Actually we could propose reasonable conformation for dictyotalide B that completely satisfied all the observed coupling patterns and NOEs of the protons, and the structure 37 (or 38) had been believed to be that of dictyotalide B, until I noticed some conflicts in the NMR chemical shifts of several protons and carbons when I compared them with those of other diterpenes from the Dictyotaceae algae (Figure 3): (i) The chemical shift of 4-C (δ 84.9) of 37 (tentative structure) is too low for acetoxy methine carbons (cf. 3923). (ii) The shift of 18-C is too high for ordinary γ-methylene carbons of α,β-unsaturated γ-lactone (cf. 27,20 39), and also the geminal coupling constant (J = 13 Hz) between the 18-methylene protons of 37 is too small (cf. 27, 39), rather resembling those of the acetoxymethylene (cf. 40,18,26 77)). (iii) The β-carbon (2-C) of 37 shows the carbon signal at about 20 ppm higher field than those of 27, and 39. On the basis of these considerations, we proposed two other structures 36 and 41 instead of 37 (or 38) for dictyotalide B. At first sight
the structures seemed to be implausible since they apparently violate Bredes' rule. The structure 41 is the case; it was impossible to construct the molecular models for 41. However, the models for 36 (or stereoisomer 42) were quite easily built,
Table 3. $^{1}H$ and $^{13}C$-NMR spectra of dictyotalide B (36)

<table>
<thead>
<tr>
<th>Carbon</th>
<th>$^{13}C$-NMR</th>
<th>$^{1}H$-NMR (500 MHz, CDCl$_3$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>141.8</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>133.3</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>50.7</td>
<td>2.52 (d, $J$ = 8.5 Hz)</td>
</tr>
<tr>
<td>4</td>
<td>84.9</td>
<td>4.73 (dd, $J$ = 3.4, 2.3 Hz)</td>
</tr>
<tr>
<td>5</td>
<td>44.2</td>
<td>a) 2.18 (dd, $J$ = 13.7, 3.4 Hz)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>b) 2.60 (dd, $J$ = 13.7, 2.3 Hz)</td>
</tr>
<tr>
<td>6</td>
<td>135.7</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>125.9</td>
<td>5.07 (brdd, $J$ = 12.1, 4.8 Hz)</td>
</tr>
<tr>
<td>8</td>
<td>29.7</td>
<td>a) 2.46 (dq, $J$ = 12.3, 3.5 Hz)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>b) 2.11 (qd, $J$ = 12.3, 3.5 Hz)</td>
</tr>
<tr>
<td>9</td>
<td>33.5</td>
<td>a) 1.87 (td, $J$ = 12.3, 3.5 Hz)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>b) 2.54 (dt, $J$ = 12.3, 3.5 Hz)</td>
</tr>
<tr>
<td>10</td>
<td>34.5</td>
<td>1.49 (m)</td>
</tr>
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<td>33.5</td>
<td>1.38 (m), 0.96 (m)</td>
</tr>
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<td>12</td>
<td>25.7</td>
<td>2.00 (m), 1.85 (m)</td>
</tr>
<tr>
<td>13</td>
<td>124.0</td>
<td>5.00 (brt, $J$ = 7 Hz)</td>
</tr>
<tr>
<td>14</td>
<td>132.0</td>
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<td>15</td>
<td>25.8</td>
<td>1.66 (brs)</td>
</tr>
<tr>
<td>16</td>
<td>17.8</td>
<td>1.57 (brs)</td>
</tr>
<tr>
<td>17</td>
<td>17.3</td>
<td>0.92 (d, $J$ = 6.6 Hz)</td>
</tr>
<tr>
<td>18</td>
<td>169.3</td>
<td>-</td>
</tr>
<tr>
<td>19</td>
<td>61.9</td>
<td>5.25 (d, $J$ = 13.3 Hz)</td>
</tr>
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<td></td>
<td></td>
<td>5.02 (d, $J$ = 13.3 Hz)</td>
</tr>
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<td>20</td>
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<td>1.38 (brs)</td>
</tr>
<tr>
<td>AcO</td>
<td>170.8</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>21.0</td>
<td>2.10 (s)</td>
</tr>
</tbody>
</table>

![NMR Spectra Diagram]
and the attention was focused on the structure 36 (or 42).
This structure was compatible with all the chemical shifts of
the protons and carbons that were argued above [(i)-(iii)] as
well as the coupling patterns of other protons. Thus, the
unusual upfield chemical shift (δ 141.8) of 1-C is interpretable by the finding that, in the molecular models, the carbonyl
group is out of the plane formed by the double bond (C1=C2).
The end absorption of the UV spectrum is also suggestive that
the lactonic carbonyl is not fully conjugated with the double
bond (cf. 27; λ_{max} (EtOH) 220 nm, 22; λ_{max} (MeOH) 226 nm).
Eventually, dicytosalide B was proved to have the structure 36
(or 42) by observing the long-range couplings between protons
and carbons: In the COLOC experiments the correlation peaks
showing the coupling between the carbonyl carbon (18-C) and the
methylene proton at 4-C were clearly observed. Also, the
couplings from the methylene protons at 19-C to the carbonyl carbon of the acetoxy group were present. These observations could eliminate the possibility of the structure 36 (or 42). The conformation 43 is the most probable one that fits the coupling patterns and NOEs found for dictyotalide B.

The $\mathcal{Z}$-configuration of $C_1$-$C_2$ was confirmed by the following chemical transformations. Dictyotalide B was saponified (NaOH/dioxane), and the product was acetylated to give a 1:2 mixture of 36 and 44. Formation of the lactone 44 is in agreement with the $\mathcal{Z}$-configuration of the 1-olefin group.

\[
\begin{align*}
\text{NaOH} & \quad \text{dioxane} \\
36 & \quad \xrightarrow{\text{Ac}_2\text{O} \quad \text{py}} \quad \text{no reaction} \\
& \quad \xrightarrow{} \\
44 & \quad \text{Ac}_2\text{O} \quad \text{py} \\
& \quad \xrightarrow{36}
\end{align*}
\]
II-D Diterpenes with a Bicyclo[7.2.0]undecane Skeleton

Further biogenetic cyclization of the xenicane skeleton has produced several very unusual diterpenes, the most striking of which are acetylcoriaceone (45) and isoacetylcoriaceone (46).

The methanol extract of *P. coriaceum* afforded a pair of isomers as very minor components after separation by column chromatography. These isomers could be separated by preparative TLC (hexane : ethyl acetate = 95 : 5, 11 developments) as viscous oils, which were designated as acetylcoriaceone (0.09% of the methanol extract) and isoacetylcoriaceone (0.07%). High resolution mass spectral analysis of acetylcoriaceone showed a molecular ion at m/e 344.233 corresponding to C\textsubscript{22}H\textsubscript{32}O\textsubscript{3}. An intense IR absorption at 1770 cm\textsuperscript{-1} and a weak but sharp signal at 1610 cm\textsuperscript{-1} suggested the existence of a highly strained enone system, which was assumed to be included in a cyclobutane ring because these IR absorptions were reasonably close to those reported for 3-methylcyclobutenone (47). A short wavelength absorption maximum (229 nm) with a small molar
absorptivity ($\varepsilon$ 6500) in the UV spectrum was also compatible with the reported value (219 nm, $\varepsilon$ 6300) of 47. The unusual downfield chemical shifts of the olefinic carbons, $\delta$ 170.3 (or 170.7) and $\delta$ 161.0, together with the upfield chemical shift of the carbonyl carbon ($\delta$ 186.1) in the $^{13}$C-NMR spectrum (Table 4) were characteristic of a cyclobutenone moiety.

The presence of an acetoxy group in acetylcoriacencnone was easily recognized from the IR bands at 1740 and 1220 cm$^{-1}$ and also the sharp singlet at $\delta$ 2.10 in the $^1$H-NMR spectrum (Table 4). The position of the acetoxy group was assumed to be adjacent to the carbonyl group of the cyclobutenone system on the basis of a downfield singlet at $\delta$ 6.02 (1H) in the $^1$H-NMR spectrum and a doublet at $\delta$ 84.8 in the $^{13}$C-NMR spectrum. These properties allowed me to deduce partial structure A. A fragment at m/e 243 (base peak) in the mass spectrum supported this partial structure.

Further analysis of the spectra of acetylcoriacencnone revealed the presence of a side chain $B$ ($^{13}$C-NMR and mass

![Diagram of molecular structure with labels and chemical shifts]
spectra) and a trisubstituted olefin having a methyl group. The configuration of the olefin was deduced to be E from the $^{13}$C chemical shift (δ 16.3) of the methyl group. In the $^1$H-NMR spectrum, the signal due to this methyl appeared relatively upfield (δ 1.41). Such shielded olefinic methyls are frequently encountered in the $^1$H-NMR spectra of sesquiterpenes that consist of medium-sized rings.²⁸

Catalytic hydrogenation of acetylcoriacenone brought about removal of the allylic acetoxy group, yielding the hexahydro derivative 48. An attempted Baeyer-Villiger reaction (MCPBA, CDCl₃, room temperature, 72 hr) resulted in recovery of 48. This
inertness is reasonable only if the carbonyl group of 48 is located close to a bulky group, the side chain. From these facts as well as biogenetic considerations, structure 45 (except the configurations of the substituents) was assumed for acetylcoryiacenone. Since hydrogenation of isoacetylcoryiacenone under the same conditions also afforded 48, the structure of this isomer was assumed to be 46.

Structures 45 and 46 were confirmed by the following experiments, carried out on the epoxides 49 and 50, which were easily obtained by autoxidation of 45 and 46. By triple

\[ \text{Diagram showing structures 49 and 50 with pertinent NMR data.} \]
<table>
<thead>
<tr>
<th>position number</th>
<th>carbon-13 chemical shift</th>
<th>proton chemical shift&lt;sup&gt;a&lt;/sup&gt;</th>
<th>proton chemical shift&lt;sup&gt;b&lt;/sup&gt;</th>
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<tbody>
<tr>
<td>1</td>
<td>161.0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>170.3&lt;sup&gt;c&lt;/sup&gt;</td>
<td>-</td>
<td>-</td>
</tr>
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<td>3</td>
<td>28.5</td>
<td>2.79 (dt, 12, 3, 4)</td>
<td>2.67 (ddd, 14, 13, 4)</td>
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<td></td>
<td></td>
<td>2.3&lt;sup&gt;d&lt;/sup&gt;</td>
<td>2.88 (br d, 14)</td>
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<tr>
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<td>1.98&lt;sup&gt;d&lt;/sup&gt;</td>
<td>1.18 (ddd, 15, 13, 10)</td>
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<td></td>
<td></td>
<td>2.28&lt;sup&gt;d&lt;/sup&gt;</td>
<td>2.28 (br d, 15, 4)</td>
</tr>
<tr>
<td>5</td>
<td>122.8</td>
<td>5.13 (dd, 11, 3)</td>
<td>2.88 (br d, 10)</td>
</tr>
<tr>
<td>6</td>
<td>140.4</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>40.2</td>
<td>1.9&lt;sup&gt;d&lt;/sup&gt;</td>
<td>2.22&lt;sup&gt;d&lt;/sup&gt;</td>
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<tr>
<td>8</td>
<td>31.6</td>
<td></td>
<td>1.85&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>9</td>
<td>43.4</td>
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<td>34.7</td>
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<td>1.7&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
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<td>12</td>
<td>25.5</td>
<td>1.85&lt;sup&gt;d&lt;/sup&gt;</td>
<td>1.85&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>13</td>
<td>124.3</td>
<td>5.01 (br t, 7)</td>
<td>5.01 (br t, 7)</td>
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<tr>
<td>14</td>
<td>131.4</td>
<td>-</td>
<td>-</td>
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<tr>
<td>15</td>
<td>25.7</td>
<td>1.67 (br s)</td>
<td>1.67 (br s)</td>
</tr>
<tr>
<td>16</td>
<td>17.6</td>
<td>1.57 (br s)</td>
<td>1.57 (br s)</td>
</tr>
<tr>
<td>17</td>
<td>17.6</td>
<td>0.91 (d, 7)</td>
<td>0.93 (d, 7)</td>
</tr>
<tr>
<td>18</td>
<td>186.1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>19</td>
<td>84.8</td>
<td>6.02 (s)</td>
<td>6.07 (s)</td>
</tr>
<tr>
<td>20</td>
<td>16.3</td>
<td>1.41 (br s)</td>
<td>1.07 (s)</td>
</tr>
<tr>
<td>AcO</td>
<td>20.8</td>
<td>2.11 (s)</td>
<td>2.08 (s)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Chemical shifts in ppm from TMS.
<sup>b</sup> Coupling constants in Hz.
<sup>c</sup> Residual errors in ppm.

70
resonance experiments, the protons on 3-C, 4-C, and 5-C of 49 could be assigned in perspective structure 51. Observation of a 6.5% NOE on 19-H (δ 6.07) upon irradiation of 3-H₉ (δ 2.88) lead to confirmation of the location of the acetoxy at 19-C. Although no NOE between 19-H and 20-methyl (δ 1.07) was found for 49, a 10% NOE was detected between the corresponding proton (δ 5.93) and methyl (δ 1.00) for the isomer 50. On the basis of these findings, the configurations of the acetoxy groups relative to 20-methyls of 49 and 50 were assigned as depicted in the respective structures. The chiroptical properties of 45 and 46 supported these assignments; the CD curves (Figure 4) of 45 [226 nm (Δε -7.8), 316 nm (Δε 1.2)] and 46 [234 nm (Δε 11.6), 317 nm (Δε -2.2)] are almost antisymmetric, showing that the Cotton effect is primarily affected by the acetoxy adjacent to the carbonyl group and that the acetoxy-cyclobutene

![Figure 4. CD spectra of acetylcoriarenone (45, —) and isoacetylcoriarenone (46, ——).](image-url)
moieties of these two isomers are in an enantiomeric relationship.

Of the possible conformations of epoxide 49, the conformer 51 (or its enantiomer) is the only one that fulfills the $^1$H-NMR properties, that is, coupling patterns, shielding of the methyl at 6-C, and NOE.

Acetylcorticenone and isoacetylcorticenone are the first representatives of a novel class of diterpenes that incorporate a cyclobutenone fused to a nine-membered ring system.
Diterpenes with a Crenulide Skeleton

Among the diterpenes found from the Dictyotaceae seaweeds, crenulides are one of the most unique groups, because they have a novel skeleton composed of a cyclooctane ring fused with a cyclopropane ring, as exemplified by acetoxycrenulide (52).23

A new compound having a crenulide skeleton was isolated from P. coriaceum, and its structure together with the stereochemical features was elucidated by spectral analyses.

By repeated column chromatography on silica gel of the methanol extract of the alga, followed by HPLC separation, a new compound, which was designated as pachylactone,29) was obtained as an oil (4 mg from 30 g of the methanol extract).

Pachylactone (53), C_{20}H_{30}O_2 (M^+, m/e 302), [\alpha]_D -23.3^\circ (c 0.18, CHCl_3), exhibits IR bands at 1755 (s) and 1660 (w) cm^{-1}, and \textsuperscript{1}H-NMR signals (90 MHz) centered at \delta 4.60 (2H, ABq, J = 16 Hz), which, coupled with the UV maximum at 228 nm (\epsilon 11700), indicate the presence of an \alpha,\beta-unsaturated \gamma-lactone. The
fragments at m/e 191 (100%) and 109 (44%) suggest that 6-methyl-5-hepten-2-yl group is included in pachylactone. Its $^{13}\text{C}$-NMR spectrum (Table 6) shows a series of signals, the chemical shifts of which correspond well to those reported for the side chain carbons. The presence of a cyclopropane ring in pachylactone is recognized by the multiplet at $\delta$ 0.11 (1H) appearing in the $^1\text{H}$-NMR spectrum (90 MHz).

Analysis of the 400 MHz $^1\text{H}$-NMR spectrum (Table 5) allowed me to propose the structure 53 for pachylactone. The upfield signal ascribable to a cyclopropane methylene proton (4-$H_b$) appears as a quartet ($J = 5$ Hz) at $\delta$ 0.11. The coupling pattern shows that this proton is equally coupled with three protons, 4-$H_a$ ($J^{\text{gem}} = 5$ Hz), 3-$H$ ($J^{\text{trans}} = 5$ Hz), and 5-$H$ ($J^{\text{trans}} = 5$ Hz). The other methylene proton signal (4-$H_a$) appears at $\delta$ 0.91 as a double triplet ($J^{\text{gem}} = 5$ Hz; $J^{\text{cis}}_{4a-3} = J^{\text{cis}}_{4a-5} = 8.5$ Hz). From these properties, it is obvious that the cyclopropane ring is cis-disubstituted.\textsuperscript{30} Decoupling
experiments showed that two other cyclopropane protons exhibit
signals at $\delta$ 1.0 and 1.7. The downfield chemical shift of the
latter suggests that the cyclopropane ring is connected with an
unsaturated moiety, the $\alpha,\beta$-unsaturated $\gamma$-lactone. By means
of 2D-correlation spectroscopy (COSY), together with decoupling
works, a tertiary carbon (6-C) 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 $\delta$ 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-$H_B$ ($\delta$ 0.11) and 19-$H_B$
($\delta$ 4.46) settled the position of the lactonic carbonyl at 18-C
(not at 19-C).

The downfield triplet ($J = 9$ Hz) at $\delta$ 2.54 is ascribable
to an allylic methine (9-H). Irradiation at this signal
simplified the multiplets at $\delta$ 1.45 (8-$H_B$) and 2.33. Inverse-
ly, irradiation at the latter multiplet ($\delta$ 2.33) simultaneously
changed the triplet at $\delta$ 2.54 into a doublet, and a doublet due
to a methyl (17-Me; $\delta$ 0.95) into a singlet. These facts show
that the multiplet at $\delta$ 2.33 is assignable to 10-H. This
unusual downfield chemical shift of 10-H, and also the rela-
tively 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 (18-C), and, at the same time, the
Table 5. $^1$H-NMR chemical shifts of pachylactone (53).

<table>
<thead>
<tr>
<th>position No.</th>
<th>$\delta$ (ppm)</th>
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</thead>
<tbody>
<tr>
<td>3</td>
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</tr>
<tr>
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</tr>
<tr>
<td>4b</td>
<td>0.11 (q, $J=5$ Hz)</td>
</tr>
<tr>
<td>5</td>
<td>1.0 (dtd, $J=10,8.5,5$ Hz)*</td>
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<td>6</td>
<td>0.85 (m)</td>
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<tr>
<td>7a</td>
<td>1.54 (m)</td>
</tr>
<tr>
<td>7b</td>
<td>1.7 (d$\delta$d, $J=12,7,2$ Hz)*</td>
</tr>
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<td>8b</td>
<td>1.45 (m)</td>
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<tr>
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</tr>
<tr>
<td>20</td>
<td>1.00 (3H,d, $J=7$ Hz)</td>
</tr>
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</table>

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

Table 6. $^{13}$C-NMR chemical shifts of 53 and isoacetoxycrenulatin (55).

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<td>162.4</td>
</tr>
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<td>3</td>
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<tr>
<td>20</td>
<td>23.3</td>
<td>23.7</td>
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</tbody>
</table>

*Assignment was confirmed by heterospin selective decoupling works. **Carbon bearing an acetoxy group.
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-Ha (δ 1.54) (NOE difference spectrum). From the considerations of all these properties, the conformation of pachylactone, as well as the relative configurations at 6-C and 9-C, was deduced as in 54. 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 C1=C2, but also above the cyclopropane ring. Molecular models show that the dihedral angles formed by 9-H and each of 10-H, 8-Hb, and 8-Ha are 150°, 170°, and 75° respectively, thus, verifying the triplet nature of 9-H. The coupling constant between 5-H and 6-H was determined to be 10 Hz by J-resolved 2D-NMR spectrum. This magnitude is quite reasonable, since these protons are in the anti-coplanar relationship in 54. Detection of NOEs between 19-Hb and 4-Hb
(2.2 Å) and also between 7-H and 9-H (2.3 Å) is a good evidence for this conformation.

Recently, the structure elucidation of isoacetoxycrenulatin (55) (except for stereochemistry) has been reported. The present diterpene, pachylactone (53), exhibits the 13C-NMR spectrum closely resembling that of 55 (Table 6), which indicated that these diterpenes have the same carbon framework, crenulatane. On the basis of the 1H-NMR data reported for isoacetoxycrenulatin (55), coupled with the considerations of the proposed conformation (54) of pachylactone, the stereochemistry of isoacetoxycrenulatin was deduced to be as illustrated in 55.
II-F Diterpenes with a Bicyclo[4.3.1]decane Skeleton

Cyclization of the xenicane skeleton with formation of a bond between carbons 7 and 18 provides the bridged bicyclic diterpenes, which have never been found thus far.

Chromatographic separation of the methanol extract of *P. coriaceum* afforded two new diterpenoids having the bicyclo[4.3.1]decane skeleton, sanadaol\(^{34}\) and acetyl-sanadaol\(^{34}\).

Sanadaol (56) showed the highest ion peak at m/e 302 corresponding to the molecular formula C\(_{20}\)H\(_{30}\)O\(_2\) in the mass spectrum. The \(^{13}\)C-NMR spectrum also supported this molecular formula. Sanadaol exhibited IR absorption bands due to a hydroxyl (3560 cm\(^{-1}\)) and an \(\alpha,\beta\)-unsaturated aldehyde (2710, 1685, 1630 cm\(^{-1}\)) groups. In the \(^1\)H-NMR spectrum (100 MHz), the aldehyde proton appeared as a singlet at \(\delta 9.47\). The chemical shift of an olefinic proton (\(\delta 6.80\)) showed that this proton was on the \(\beta\)-carbon of the \(\alpha,\beta\)-unsaturated aldehyde, and had the cis-relationship with the aldehyde group. The olefin signal was split into a triplet (\(J = 3\) Hz) by coupling with methylene protons which appeared at \(\delta 2.6\) as a multiplet. More detailed experiments by means of a 270 MHz NMR instrument (Table 7) revealed that the aldehyde and the olefinic protons were weakly coupled (\(J = 1\) Hz) with each other. The signals due to the methylene protons now appeared as well-separated peaks at \(\delta 2.75\) and 2.56 (each 1H). Double resonance experi-
ments showed that each of them was equally coupled with the olefinic proton (δ 6.80) with the coupling constant of 3.5 Hz. Furthermore, the signal at δ 2.75 was found to be coupled with a methine proton at δ 2.88, suggesting part structure A.

The methine proton resonating at δ 2.88 should be adjacent to an exomethylene group, the signal of which was sharpened on irradiation at the methine signal. Moreover, since this methine proton was coupled with a proton at δ 3.78 (J = 4.3 Hz), the methine group should be bonded to another tertiary carbon bearing a hydroxy group. This carbinyl proton was coupled with two other protons, a hydroxy (δ 2.10, J = 9.0 Hz) and another down-field methine (δ 3.19, J = 5.0 Hz) protons.
Observation of a long range coupling between this methine proton (δ 3.19) and the aforementioned proton at δ 2.75 (J = 1.5 Hz) allowed the part structure A to be expanded to B.

Presence of fragment C in sanadaol was evident from its $^1$H-NMR and mass spectra, although a signal ascribable to a secondary methyl group appeared at considerably upfield (δ 0.77) in contrast to those of dictyodial (21)$^{17}$ (δ 0.89) and dictyolactone (22)$^{17}$ (δ 0.95), indicating that the environment of the side chain of sanadaol was different from those of the two diterpenes. Combination of the part structures B, C, and remaining two methylene units on the basis of the consideration of the $^{13}$C-NMR spectrum and the coupling constants lead to the structure 56 for sanadaol including relative stereochemistry.

![Chemical structure diagram]

Orientation of the side chain on 3-C was verified from a small coupling constant (1 Hz) between 2-H (δ 3.19) and 3-H (δ 1.6). The configuration of the hydroxy group at 18-C was determined to be as described in 57 by means of a lanthanide shift reagent. That is, on addition of 2.6 molar equivalents
Table 7. $^1$H-NMR spectrum (270 MHz, CDCl$_3$) of sanadaol (56).

<table>
<thead>
<tr>
<th>Proton</th>
<th>Chemical shift (δ)</th>
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<tbody>
<tr>
<td>H-2</td>
<td>3.19 (dddd, J=5.0,1.5,1.1 Hz)</td>
</tr>
<tr>
<td>3</td>
<td>1.6 (obscured by Me signals)</td>
</tr>
<tr>
<td>4</td>
<td>1.3 (2H, m)</td>
</tr>
<tr>
<td>5</td>
<td>2.25 (2H, m)</td>
</tr>
<tr>
<td>7</td>
<td>2.88 (dddt, J=7.0,4.3,1,1 Hz)</td>
</tr>
<tr>
<td>8a</td>
<td>2.75 (dddd, J=21.0,7.0,3.5,1.5 Hz)</td>
</tr>
<tr>
<td>8b</td>
<td>2.56 (dd, J=21.0,3.5 Hz)</td>
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<tr>
<td>9</td>
<td>6.80 (td, J=3.5,1 Hz)</td>
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<td>10</td>
<td>1.6 (obscured by Me signals)</td>
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<td>12</td>
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<td>5.16 (t, J=7.0 Hz)</td>
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<td>1.69 (s)</td>
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<tr>
<td>16</td>
<td>1.62 (s)</td>
</tr>
<tr>
<td>17</td>
<td>0.77 (d, J=6.2 Hz)</td>
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<tr>
<td>18</td>
<td>3.78 (dddd, J=9.0,5.0,4.3 Hz)</td>
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<td>19</td>
<td>9.47 (d, J=1 Hz)</td>
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<tr>
<td>20</td>
<td>4.90 (2H, td, J=1,1 Hz)</td>
</tr>
<tr>
<td>OH</td>
<td>2.10 (d, J=9.0 Hz)</td>
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</table>

![Diagram of sanadaol molecule with labels and interactions]

<table>
<thead>
<tr>
<th>Eu(fod)$_3$shift</th>
<th>Δδ</th>
</tr>
</thead>
<tbody>
<tr>
<td>$H_a$</td>
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</tr>
<tr>
<td>$H_b$</td>
<td>1.10</td>
</tr>
<tr>
<td>$H_c$</td>
<td>0.85</td>
</tr>
<tr>
<td>$H_d$</td>
<td>0.73</td>
</tr>
</tbody>
</table>
of Eu(fod)$_3$, the signal due to the exomethylene protons (20-H) shifted to downfield much more significantly (δ 1.58 for 20-$_H_a$ and 1.10 for 20-$_H_b$) than those of 8-$_H$ (δ 0.73) and 19-$_H$ (δ 0.85).

The structure 56 of sanadaol was unambiguously confirmed by the following chemical conversion. A solution of dictyodial (21) in dichloromethane was allowed to stand with silica gel at room temperature for 12 hr, affording sanadaol. An acid-catalyzed ene reaction might be involved in this transformation.19)

**Acetylisanadaol (58)** exhibited a molecular ion perk at m/e 344 corresponding to an acetate of sanadaol (56) in the mass spectrum. The IR spectrum (1730, 1690, 1630 cm$^{-1}$) suggested the occurrence of an α,β-unsaturated aldehyde. The $^1$H-NMR spectrum was essentially the same as that of sanadaol except the presence of an acetyl signal (δ 2.03) and downfield chemical shift (δ 4.75) of a methine proton on the carbon bearing an oxygen function. Indeed, acetylation of 56 with acetic anhydride and pyridine gave rise to a product, the spectral data of which were identical with those of acetyl-sanadaol, thus confirming the structure 58.

The bicyclo[4.3.1]decane skeleton of sanadaol (56) and acetylisanadaol (58) has never been found in natural products thus far. Formation of sanadaol from dictyodial (21) on silica gel suggests the possibility that sanadaol could be an artifact which was produced during chromatographic separation. However,
existence of acetylsanadaol, which is without doubt a natural product, in the methanol extract of the alga, shows that sanadaol is, at least in part, of a natural origin.

The conversion of dictyodial (21) was carried out under extremely mild reaction conditions. Thus, when 21 (230 mg) was allowed to stand with silica gel (10 g; Merck, Kieselgel 60 F<sub>254</sub>, Art. 7734) in dichloromethane (10 ml) at room temperature for 12 hr, there was obtained two unknown products, A (30 mg, 13%) and B (28 mg, 12%), together with sanadaol (56; 74 mg, 33%).

![Diagram of molecules 21 and 56]

**Compound A** has the same molecular composition (C<sub>20</sub>H<sub>30</sub>O<sub>2</sub>) as that of sanadaol (56). Of the two aldehydic proton signals at δ 10.13 (d, J = 3 Hz) and 9.28 (s) in the <sup>1</sup>H-NMR spectrum of dictyodial (21), the signal corresponding to the former doublet is absent in the <sup>1</sup>H-NMR spectrum of compound A. The unconjugated aldehyde group at 18-C and the olefin group at 6-C must be involved in the reaction, because the signals due to the olefinic proton at 7-C and the olefinic methyl at 6-C are not present in the <sup>1</sup>H-NMR spectrum of compound A. The <sup>1</sup>H-NMR
spectrum considerably resembles that of sanadaol (56), except for a sharp singlet at \( \delta 1.36 \) due to a tertiary methyl group instead of the exo-methylene signals in 56. On the basis of these data, the structure 59 was deduced for compound A. The downfield chemical shifts of the signals assignable to 18-H (\( \delta 4.40 \)) and 6-C (\( \delta 90.9 \)) in the NMR spectra of the compound A are compatible with the oxetane structure in 59. It should be emphasized that an oxetane was formed under very mild conditions, that is, in the absence of light or strong acids.

Compound B (C_{20}H_{30}O_{2}) is also an isomer of sanadaol (56). In fact, the \( ^1H \)-NMR spectrum of this compound is extremely similar with that of 56. The only significant difference between their spectra is the appearance of an olefinic methyl signal (\( \delta 1.76 \)) in the spectrum of B instead of the exo-methylene signal in that of 56. This spectral property, and also other spectral data allowed me to deduce the structure 60 for compound B, which was designated as isosanadaol.
The relative configuration of the hydroxy group at 18-C was determined as depicted in structure 60 by use of a lanthanide shift reagent in $^1$H-NMR works; on addition of 0.13 molar equivalent of Eu(fod)$_3$ the signal due to 5-H shifts to downfield more significantly than the signal due to 9-H ($\delta$ 0.39).

The reaction may proceed via the conformer M to the cation N, which is the common intermediate leading to 56, 59, and 60. Noteworthy is the fact that all the products have $R^*$ (relative) configuration at 18-C. No epimer at 18-C has been isolated so far.

Fukurinal (61),$^{26}$ a diterpene, was recently isolated from Dilophus okamurai, with the same carbon skeleton as sanadaol (56). The structure was proposed from spectroscopic analyses, but the configuration at 10-C remained undetermined. In my studies on acid-catalyzed cyclization of dictyodial derivatives,$^{19}$ I have now synthesized fukurinal (61) from dictyodi-
acetal (62), the stereochemistry of which was firmly established. This transformation chemically confirmed the complete stereochemistry of fukurinal (61). On mild acid treatment, dictyodial (21) was converted into sanadaol (56) by transannular cyclization. Under the same conditions, dictyodiacetal (62) was not converted into a bicyclic compound, but, instead, was hydrolyzed to a dialdehyde (63). On the other hand, treatment of dictyodiacetal with boron trifluoride etherate, for 30 min at room temperature, afforded three cyclization products, A (25%), B (8%), and C (5%).

**Compound A,** C_{22}H_{32}O_{4}, was a colorless oil. IR bands at 1735 and 1235 cm\(^{-1}\), as well as the \(^1\)H-NMR signals at \(\delta\) 1.92 (3H, s) and 5.0 (1H, m), indicated that the acetoxy group remained intact. Presence of an \(\alpha,\beta\)-unsaturated aldehyde moiety was deduced from IR bands at 1695 and 1635 cm\(^{-1}\), and also by \(^1\)H-NMR signals at \(\delta\) 9.50 (1H, s, CHO). Disappearance of one acetal (or aldehyde) group in dictyodiacetal (62) and the appearance of new signals at \(\delta\) 4.96 (2H, s, =CH\(_2\)) and 3.88 (1H, m, CH-O) suggested that an intramolecular ene-type reaction occurred between the aldehyde and methyl vinyl groups affording a bicyclic compound 64. Acetylation of compound 64 afforded an acetate 61 with \(^1\)H and \(^13\)C-NMR properties identical in all respects to those reported for fukurinal. Thus, the configuration of fukurinal at 2, 3, 4-C, and especially at 10-C, have been established to be identical with those of dictyodi-
diacetal (62).

Compound B, C_{20}H_{28}O_{2}, lacked an acetoxy group and, instead, revealed a UV absorption maximum at 258 nm due to a homodiene chromophore, which was confirmed by $^1$H-NMR signals at $\delta$ 5.72 (1H, d, $J = 8$ Hz; 4-H) and 5.79 (1H, d, $J = 8$ Hz; 5-H). Furthermore, the $^1$H-NMR spectrum exhibited a broad singlet ascribable to a highly deshielded olefinic methyl (20-CH$_3$) at 1.89, as well as signals due to an $\alpha$, $\beta$-unsaturated aldehyde moiety at $\delta$ 9.40 (1H, s) and 6.72 (1H, bs). These data provide structure 65 for compound B. Configuration of the hydroxy group at the newly formed chiral center 18-C was deduced from the coupling pattern of 18-H ($\delta$ 4.01, dd, $J = 6, 3.5$ Hz).

Compound C, C$_{22}$H$_{34}$O$_{5}$, showed the $^1$H-NMR spectrum similar to compound 64, except for the appearance of sharp singlets at $\delta$ 1.22 (3H) and 1.24 (3H) instead of olefinic methyl signals (1.64 and 1.70) as in bicyclic compound 64. These properties suggested that the side chain olefinic bond was hydroxylated in compound C. A hydroxy group at 14-C was confirmed by the fragment m/e 319 (M$^+$-C$_3$H$_7$O) in the mass spectrum of compound C, allowing the structure to be assigned as 66. Configuration of 18-C was deduced from the coupling pattern of 18-H ($\delta$ 3.88, dd, $J = 5, 3$ Hz) in the $^1$H-NMR spectrum.
II-G Biogenesis

The biogenesis pathways of the diterpenoids reported in this chapter are illustrated in Figure 5.

Geranylgeraniol can produce the "germacrane-like" diterpenoids (described in II-A) by 1-C to 10-C bond formation. Further ring closure at 2-C to 6-C would yield the perhydroazulene skeleton found in pachydictyol A (II-B). Rearrangement of 10-C to 2-C in the cyclodecane ring can produce the xenicane skeleton found in dictyodial (II-C). Furthermore, ring closure of the xenicane ring at 1-C to 2-C, 4-C to 6-C, and 1-C to 6-C gives the bicyclo[7.2.0]undecane (II-D), the crenulide (II-E), and the bicyclo[4.3.1]decane (II-F) skeletons, respectively.
Figure 5.

MVA →

\[ \text{dilophol} \]
\[ \text{dictyodial} \]
\[ \text{acetylcoriacecenone} \]
\[ \text{pachylactone} \]

\[ \text{C}_2\text{-C}_6 \]
\[ \text{C}_1\text{-C}_{10} \]
\[ \text{C}_2\text{-C}_{10} \]
\[ \text{C}_1\text{-C}_{20} \]
\[ \text{C}_4\text{-C}_6 \]
EXPERIMENTAL

Infrared spectra were recorded on a HITACHI 215 spectrophotometer and ultraviolet spectra were recorded on a HITACHI 340 spectrophotometer. Optical rotations were recorded on a JASCO DIP-181 polarimeter, using a 10-cm microcell. $^1$H-NMR spectra were recorded on JEOL JNM-MH-100, JEOL JNM-FX-90Q, JEOL JNM-GX-400, and Bruker AM-500 spectrometers; chemical shifts are reported relative to Me$_4$Si(δ 0), and coupling constants are given in hertz. $^{13}$C-NMR spectra were recorded on JEOL JNM-FX-90Q, JEOL JNM-GX-400, and Bruker AM-500 spectrometers. Low-resolution mass spectra were obtained from a HITACHI RMU-6M mass spectrometer. CD spectra were recorded on JASCO J-20, and J-20C polarimeters.

Algal collection, extraction, and isolation of diterpenoids. Pachydictyon coriaceum was collected in June 1981 at the Izu-Shimoda beach, and Dictyota dichotoma was obtained at Yagachi, Okinawa, in June 1983. The seaweeds were soaked in MeOH immediately after the collection and allowed to stand for 1 week. The MeOH was decanted, and the residual material was again extracted with fresh MeOH for 1 week. The combined MeOH extracts were concentrated in vacuo, and the residue was successively washed with hexane, dichloromethane, and ethyl acetate. The hexane extract was concentrated, and the residue was fractionally separated by chromatography on
silica gel (Merck, Kieselgel 60, Wakogel C-300), and further purified by preparative TLC (Merck, Kieselgel 60, GF₃₄₀) and HPLC (LS-410K, LICHrosorb SI-60).

**Acetylations.** All acetylations were conducted in a similar fashion. Acetic anhydride was added to a solution of the natural product in pyridine, and the reaction mixture was allowed to stand at room temperature overnight. The excess reagents were then removed *in vacuo* to yield the acetylated products, which were purified, when necessary, by preparative TLC.

3-Hydroxyaceteyldilophol (4). $^1$H-NMR(90 MHz,CDCl₃) $\delta$

0.96(3H,d,J=7 Hz), 1.50(3H,bs), 1.60(3H,bs), 1.68(6H,bs),
2.10(3H,s), 4.36(1H,t,J=3 Hz), 5.1-5.5(3H,m), 5.68(1H,dd,J=7, 2 Hz).

Dilophol acetate (5). MS m/e 332(M⁺), 290, 272,
161(base), 159, 81, 69; $^1$H-NMR(90 MHz,CDCl₃) $\delta$

0.93(3H,d,J=6 Hz), 1.50(3H,bs), 1.56(6H,bs), 1.65(3H,bs), 1.96(3H,s),
4.95(2H,m), 5.05(1H,dt,J=7 Hz), 5.56(1H,dd,J=8 Hz); $^{13}$C-
NMR(22.5 MHz,CDCl₃) $\delta$ 16.6, 17.2, 17.7, 21.3, 24.5, 25.8, 34.3,
72.8, 124.8, 131.3, 134.1, 170.7. Other signals were broad.

[Eu(fod)$_3$] shift of obscuronatin (3). $\Delta \delta$ values
(ppm,CDCl₃) on addition of 1.4 molar equivalent of Eu(fod)$_3$:

93
2.82(4-Me), 2.55(3-H), 2.46(6-H), 1.85(2-H), 1.55(5-H), 1.11(1-H). Other signals did not show significant shifts.

**Acetyldiclytol C (16).** MS m/e 288(M⁺-60), 270, 255, 159(base); ¹H-NMR(100 MHz,CDC₁₃) δ 0.96(3H,d, J=6 Hz), 1.49(3H,s), 1.58, 1.66, 1.82(each 3H,bs), 1.97(3H,s), 3.85(1H,bd, J=8 Hz), 5.07(1H,bt, J=7 Hz), 5.23(1H,bs); ¹³C-NMR(22.5 MHz,CDC₁₃) δ 16.3(q), 17.5(q), 17.7(q), 19.7(t), 22.5(q), 25.6(t), 25.7(q), 26.2(q), 33.0(t), 34.5(d), 34.9(t), 40.5(t), 49.7(d), 51.7(d), 52.2(d), 74.6(d), 84.4(s), 123.1(d), 124.7(d), 131.5(s), 142.4(s), 170.4(s).

**Isopachydictyol A (18).** MS m/e 288(M⁺), 270, 159(base), 157; ¹H-NMR(90 MHz,CDC₁₃) δ 0.95(3H,d, J=6 Hz), 1.58(3H,bs), 1.67(3H,bs), 1.83(3H,bs), 3.90(1H,m), 5.10(1H,bt, J=7 Hz), 5.33(1H,bs), 5.47(1H,bd, J=8 Hz); ¹³C-NMR(22.5 MHz,CDC₁₃) δ 142.9(s), 138.7(s), 131.5(s), 126.1(d), 124.9(d), 124.3(d), 74.7(d), 57.6(d), 47.0(d), 46.2(d), 35.5(t), 34.9(t), 33.9(d), 25.7(q), 25.6(t), 24.6(t), 23.1(q), 17.7(q), 17.6(q), 16.3(q).

**Hydroxydictyoxide (19).** ¹H-NMR(90 MHz,CDC₁₃) δ 0.88(3H,d, J=6 Hz), 1.38(3H,s), 1.57, 1.65, 1.81(each 3H,bs), 2.34(1H,dd, J=11, 4 Hz), 3.30(1H,bd, J=11 Hz), 4.05(1H,d, J=3.5 Hz), 4.48(1H,dd, J=4, 2.5 Hz), 5.06(1H,bt, J=7 Hz), 5.67(1H,m); ¹³C-NMR(22.5 MHz,CDC₁₃) δ 147.0(s), 134.1(d), 131.5(s), 124.7(d), 77.1(d), 75.0(s), 70.6(d), 62.9(d), 57.2(d), 39.3(t), 94
38.1(d), 37.2(d), 34.5(t), 26.2(t), 25.7(q), 21.5(q), 20.3(t), 17.8(q), 16.5(q), 16.3(q).

**Acetyldictyonal (24).** UV(EtOH) 230 nm; MS m/e 346(M⁺), 328, 286, 243, 175, 149, 109, 82(base), 69; ¹H-NMR(100 MHz,CDCl₃) δ 0.86(3H,d,J=7 Hz), 1.57, 1.66, 1.77(each 3H,bs), 1.97(3H,s), 2.76(1H,dt,J=8 Hz), 4.5(2H,m), 5.1(1H,dt,J=7 Hz), 5.36(1H,dd,J=10 Hz), 6.80(1H,dd,J=8, 4 Hz), 9.40(1H,bs); ¹³C-NMR(25 MHz,CDCl₃) δ 16.8(q), 17.3(q), 17.7(q), 21.1(q), 25.7(q), 26.2(t), 28.5(t), 29.1(t), 32.1(d), 38.0(t), 41.4(t), 42.3(d), 46.9(d), 63.1(t), 122.1(d), 124.9(d), 130.9(s), 138.3(s), 150.1(s), 156.9(d), 170.8(s), 195.9(d).

**Acetal (26a).** MS m/e 348(M⁺), 316, 284, 173, 159, 145, 109(base), 97, 69; ¹H-NMR(100 MHz,CDCl₃) δ 0.88(3H,d,J=6 Hz), 1.58, 1.68, 1.73(each 3H,bs), 3.26, 3.33(each 3H,s), 5.01(1H,s), 5.10(1H,s), 5.15(1H,dt,J=7 Hz), 5.5(1H,dd,J=10, 4 Hz), 5.80(1H,dd,J=7 Hz); ¹³C-NMR(22.5 MHz,CDCl₃) δ 17.1(2xq), 17.6(q), 25.7(q), 25.9(t), 28.2(t), 30.4(t), 31.5(d), 38.4(t), 40.6(t), 46.9(d), 51.6(d), 54.5(q), 54.7(q), 107.3(2xd), 125.0(d), 125.4(d), 126.2(d), 130.8(s), 135.0(s), 146.2(s).

**Acetal (26b).** ¹H-NMR(100 MHz,CDCl₃) δ 0.93(3H,d,J=6 Hz), 1.61, 1.69, 1.72(each 3H,bs), 3.32, 3.47(each 3H,s), 5.10(1H,s), 5.1(1H,dt,J=7 Hz), 5.27(1H,bs), 5.40(1H,dd,J=10, 4 Hz), 5.88(1H,dd,J=7 Hz); ¹³C-NMR(25 MHz,CDCl₃) δ 17.2(q)

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17.7(q), 18.1(q), 25.6(q), 26.1(t), 28.4(t), 29.7(t), 31.4(d),
37.8(t), 40.5(t), 46.0(d), 53.4(d), 54.3(q), 55.4(q),
106.4(2xd), 124.6(d), 124.9(d), 125.8(d), 131.1(s), 135.0(s),
145.9(s).

**Neodictyolactone (27).** MS m/e 302(M⁺), 287, 257(base),
201, 191, 187, 147, 145, 109, 82, 69; ¹H-NMR(400 MHz,CDCl₃) δ
0.98(3H,d,J=6.5 Hz,17-H), 1.26, 1.54, 1.64(each 3H,bs,20,16,15-
H), 4.56, 4.60(each 1H,d,J=17 Hz,19-H), 4.98(1H,dt,J=7 Hz,13-
H), 5.22(1H,dd,J=12, 4 Hz,7-H); ¹³C-NMR(100 MHz,CDCl₃) δ
15.8(q,20-C), 17.6(q,16-C), 18.0(q,17-C), 25.0*(t,12-C),
25.6(q,15-C), 25.8*(t,8-C), 28.4(t,9-C), 32.1(t,4-C),
33.1(d,10-C), 35.2(t,11-C), 40.5(t,5-C), 43.1(d,3-C),
71.1(t,19-C), 123.5(d,7-C), 124.7(d,13-C), 131.1(s,14-C),
133.2(s,2-C), 140.0(s,6-C), 157.4(s,1-C), 173.8(s,18-C).

**18-Acetoxydictyolactone (31).** MS m/e 360(M⁺), 343, 300,
257, 229, 137, 109, 82, 81, 69; ¹H-NMR(90 MHz,CDCl₃) δ
1.03(3H,d,J=6 Hz,17-H), 1.57, 1.67, 1.69(each 3H,bs,16,15,20-
H), 2.55(1H,bs,2-H), 2.8-3.4(2H,m,8-H), 5.03(1H,dt,J=7 Hz,13-
H), 5.37(1H,bbd,J=11, 5 Hz,7-H), 6.68(1H,s,18-H),
7.06(1H,bbd,J=7, 3 Hz,9-H); ¹³C-NMR(22.5 MHz,CDCl₃) δ 17.3*(17-
C), 17.6*(20-C), 17.7(16-C), 21.0(AcO), 25.7(15-C), 26.0(12-C),
29.1(4-C), 30.0(8-C), 32.9(10-C), 37.7(11-C), 40.1(5-C),
47.0(2-C), 50.9(3-C), 96.0(18-C), 122.8(7-C), 124.0(13-C),
131.9(14-C), 132.4(1-C), 136.9(6-C), 143.1(9-C).

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4-Acetoxydictyolactone (32). MS m/e 360(M⁺), 318, 300, 165, 136, 109, 82, 69; ¹H-NMR(500 MHz,CDCl₃) δ 0.90(3H,d,J=6.7 Hz,17-H), 1.54, 1.64, 1.78(each 3H,d,J=1.5 Hz,16,15,20-H), 1.88(2H,m,12-H), 2.03(3H,s,Ac), 2.10(1H,dd,J=2.3, 1.5 Hz,3-H), 2.17(1H,ddd,J=13.8, 4.5, 1.0 Hz,5-Hₐ), 2.47(1H,dd,J=13.8, 2.3 Hz,5-Hₐ), 2.99(1H,ddd,J=17.6, 7.5, 4.0, 1.0 Hz,8-Hₐ), 3.19(1H,ddt,J=17.6, 11.6, 2.2 Hz,8-Hₐ), 3.36(1H,bdt,d,J=7.7, 2.2, 1.6 Hz,2-H), 4.10(1H,dd,J=9.6, 7.7 Hz,18-Hₐ), 4.44(1H,dd,J=9.6, 1.6 Hz,18-Hₐ), 4.99(1H,t,septet,J=7.1, 1.5 Hz,13-H), 5.27(1H,dd,J=4.5, 2.3 Hz,4-H), 5.36(1H,bdd,J=11.6, 4.0 Hz,7-H), 6.95(1H,dt,J=7.5, 2.2 Hz,9-H); ¹³C-NMR(125 MHz,CDCl₃) δ 172.9*(19-C), 169.8*(AcO), 139.8(9-C), 134.9(1-C), 134.9(6-C), 132.1(14-C), 126.5(7-C), 123.8(13-C), 75.6(4-C), 68.1(18-C), 49.8(3-C), 45.1(5-C), 37.6(11-C), 36.7(2-C), 32.3(10-C), 29.5(8-C), 25.8(12-C), 25.7(15-C), 21.5(AcO), 19.7(20-C), 17.8(16-C), 17.4(17-C).

Isodictyoacetal (33). IR(CCl₄) 1090, 1045, 925 cm⁻¹; MS m/e 318(M⁺), 286, 243, 215, 205, 203, 147, 133, 109, 107, 69; ¹H-NMR(90 MHz,CDCl₃) δ 0.91(3H,d,J=6 Hz,17-H), 1.58, 1.66, 1.71(each 3H,bs,16,15,20-H), 2.26(1H,bs,2-H), 3.24(3H,s,OMe), 4.29(2H,bs,19-H), 5.07(1H,s,18-H), 5.07(1H,brt,J=7 Hz,13-H), 5.40(1H,bdd,J=11, 4 Hz,7-H), 5.50(1H,m,9-H); ¹³C-NMR(22.5 MHz,CDCl₃) δ 17.2(17-C), 17.7(16-C), 17.7(20-C), 25.7(15-C), 26.3(12-C), 28.4(4-C), 29.8(8-C), 31.6(10-C), 38.1(11-C), 40.7(5-C), 45.9(2-C), 53.0(3-C), 54.3(MeO), 71.1(19-C), 97.
107.4(18-C), 119.0(9-C), 124.8(13-C), 125.8(7-C), 131.2(14-C), 134.6(6-C), 146.1(1-C).

Isoacetylcoriaceousone (46). UV(ETH0) 229 nm(ε 6100);
IR(CCL4) 1765, 1740, 1610, 1220, 1020 cm⁻¹; MS m/e 344(M⁺), 302, 274, 243(base), 163, 147, 109, 69; ¹H-NMR(400 MHz,CDCl₃) δ 0.96(3H,d,J=6.5 Hz,17-H), 1.35, 1.58, 1.68(each 3H,bs,20,16,15-H), 2.10(3H,s,Ac), 2.67(1H,dd,J=12, 3 Hz,3-H), 5.07(1H,dt,J=7 Hz,13-H), 5.19(1H,dd,J=10, 4 Hz,5-H), 5.92(1H,s,19-H); ¹³C-NMR(22.5 MHz,CDCl₃) δ 16.2(q), 17.8(2xq), 20.9(q), 23.8(t), 25.4(t), 25.7(q), 28.1(t), 32.7(t), 34.5(d), 34.9(t), 40.4(t), 43.6(d), 84.5(d), 123.6(d), 124.7(d), 131.4(s), 140.3(s), 163.7(s), 170.6(s), 172.9(s), 187.0(s).

Sanadaol (56). MS m/e 302(M⁺), 284, 273, 269, 173, 145, 109, 82, 69(base); ¹³C-NMR(25 MHz,CDCl₃) δ 193.1(d), 150.5(d), 146.4(s), 143.9(s), 130.8(s), 125.3(d), 116.5(t), 68.9(d), 46.0(d), 39.2(d), 37.7(d), 36.2(d), 35.9(t), 31.9(t), 29.9(t), 25.7(q), 25.4(t), 24.2(t), 17.7(2xq).

Acetylsanadaol (58). MS m/e 344(M⁺), 326, 284, 266, 173, 145, 109, 82, 69; ¹H-NMR(100 MHz,CDCl₃) δ 0.72(3H,d,J=6 Hz), 1.58, 1.66(each 3H,bs), 2.03(3H,s), 4.73(2H,bs), 4.75(1H,m), 5.1(1H,dt,J=7 Hz), 6.76(1H,t,J=3.5 Hz), 9.42(1H,s); ¹³C-NMR(22.5 MHz,CDCl₃) δ 192.6(d), 170.3(s), 150.3(d), 146.9(s), 143.2(s), 131.0(s), 125.1(d), 115.4(t), 72.4(d), 42.4(d), 98
39.5(d), 37.2(d), 36.0(d), 35.9(t), 32.7(t), 30.5(t), 25.7(q), 25.3(t), 24.6(t), 21.3(q), 17.7(q), 17.4(q).

**Compound A (59).** MS m/e 302(M⁺), 284, 173, 145, 109, 82, 69(base); UV(MeOH) 232 nm(ε 16200); IR(CCl₄) 2720, 1685, 1630, 1150, 960 cm⁻¹; ¹H-NMR(100 MHz,CDCl₃) δ 0.61(3H,d,J=6 Hz,17-H), 1.36(3H,s,20-H), 1.59, 1.66(each 3H,bs,16,15-H), 2.47(2H,dd,J=7, 4 Hz,8-H), 2.6(1H,m,3-H), 3.22(1H,dt,J=8, 7 Hz,7-H), 3.58(1H,dd,J=7, 3.5 Hz,2-H), 4.40(1H,dd,J=8, 7 Hz,18-H), 5.07(1H,qt,J=7 Hz,13-H), 6.90(1H,t,J=4 Hz,9-H), 9.47(1H,s,19-H); ¹³C-NMR(22.5 MHz,CDCl₃) δ 193.1(d), 151.9(d), 142.4(s), 130.9(s), 125.0(d), 90.9(s), 75.1(d), 40.6(d), 40.3(d), 37.7(d), 36.8(t), 35.7(t), 35.1(d), 30.7(q), 26.0(t), 25.7(q), 24.5(t), 21.3(t), 17.7(q), 16.1(q).

**Compound B (60).** MS m/e 302(M⁺), 284, 202, 173, 145, 109, 82, 69(base); UV(MeOH) 229 nm(ε 19800); IR(CCl₄) 3600-3100(br), 2720, 1690, 1635, 1155, 1065, 1045 cm⁻¹; ¹H-NMR(100 MHz,CDCl₃) δ 0.64(3H,d,J=6 Hz,17-H), 1.60, 1.66, 1.76(each 3H,bs,16,15,20-H), 2.65(2H,bs,8-H), 3.32(1H,dd,J=5 Hz,2-H), 3.80(1H,qt,J=5 Hz,18-H), 5.10(1H,qt,J=7 Hz,13-H), 5.57(1H,m,5-H), 6.88(1H,t,J=3 Hz,9-H), 9.43(1H,s,19-H); ¹³C-NMR(22.5 MHz,CDCl₃) δ 193.0(d), 152.6(d), 142.3(s), 139.1(s), 131.0(s), 125.9(d), 125.0(d), 69.5(d), 42.5(d), 40.9(d), 36.9(d), 36.6(t), 35.8(d), 33.3(t), 28.3(q), 25.7(q), 25.6(t), 24.9(t), 17.7(q), 17.2(q).
Compound A (64). MS m/e 360(M+), 342, 300, 218, 171, 143, 109, 82(base), 69; IR(CCl4) 1735, 1695, 1635, 1235 cm⁻¹;
1H-NMR(90 MHz,CDCl₃) δ 0.80(3H,d,J=7 Hz,17-H), 1.64, 1.70(each 3H,bs,16,15-H), 1.92(3H,s,Ac), 3.88(1H,m,18-H), 4.96(2H,s,20-H), 5.0-5.4(2H,m,4,13-H), 6.70(1H,m,9-H), 9.50(1H,s,19-H).

Compound B (65). MS m/e 300(M+,base), 143, 82, 69;
UV(EtOH) 229, 258 nm; 1H-NMR(400 MHz,CDCl₃) δ 1.02(3H,d,J=6.5 Hz,17-H), 1.62, 1.67, 1.89(each 3H,bs,16,15,20-H), 2.72(3H,m,7,8-H), 3.70(1H,dd,J=6 Hz,2-H), 4.01(1H,dd,J=6.0, 3.5 Hz,18-H), 5.15(1H,dt,J=7 Hz,13-H), 5.72(1H,d,J=8 Hz,4-H*), 5.79(1H,d,J=8 Hz,5-H*), 6.72(1H,bs,9-H), 9.40(1H,s,19-H).

Compound C (66). MS m/e 360(M+), 343, 300, 218, 189, 176, 109, 82(base), 69; 1H-NMR(400 MHz,CDCl₃) δ 0.79(3H,d,J=7 Hz,17-H), 1.22, 1.24, 1.91(each 3H,s,15,16-H,Ac), 2.44(1H,dd,J=20, 4 Hz,8-H), 2.79(1H,dt,J=20 Hz,8-H), 2.85(1H,m,7-H), 3.08(1H,dd,J=13, 10 Hz,5-H), 3.17(1H,dd,J=5 Hz,2-H), 3.88(1H,dd,J=5, 3 Hz,18-H), 4.96(2H,s,20-H), 5.06(1H,m,4-H), 6.71(1H,bs,9-H), 9.50(1H,s,19-H).

Hydrolysis of dilophol acetate (5) to dilophol (1). A 20 % methanolic KOH solution was added to a solution of 5 (16 mg) in MeOH. The reaction mixture was allowed to stand at r.t. for 4 hr. The solution was diluted with water and extracted with ether. The ether layer was washed with brine and evaporated,
and the residue was purified by preparative TLC to obtain 1 (7.3 mg).

**Benzoylation of acetoxypachydiol (7) to 8.** Excess benzoyl chloride was added to a solution of 7 (3.6 mg) in pyridine, and the reaction mixture was stirred at r.t. for 4.5 hr. The reaction was quenched by the addition of water, and the solution was extracted with ether. The ether layer was washed with brine, dried over MgSO₄, and concentrated. The residue was purified by column chromatography and preparative TLC to give 8 (2.5 mg): C₃₆H₄₄O₆, ¹H-NMR(90 MHz,CDCl₃) δ 0.85(3H,d,J=7 Hz,18-H), 1.56, 1.63(each 3H,bs,17,16-H), 1.97(6H,s,Ac), 2.7, 3.4(each 1H,m,2-H), 4.60, 4.72(each 1H,d,J=12 Hz,20-H), 5.03(1H,dt,J=7 Hz,14-H), 5.33(1H,dt,J=10 Hz,1-H), 5.78(2H,bs,5,6-H), 6.33(1H,dd,J=9, 4 Hz,3-H), 7.3(6H,m,Ar), 7.8(4H,m,Ar).

**Acetylation of acetyldictyol C (16) to 17.** A solution of 16 in pyridine and acetic anhydride was refluxed at 100 °C in a sealed tube for 24 hr. The excess reagents were removed in vacuo to give the diacetate 17: C₂₄H₃₈O₄, MS m/e 330(M⁺-AcOH), 270, 255, 199, 185, 159(base), 145, 131, 69; IR(CCl₄) 1730, 1240 cm⁻¹; ¹H-NMR(60 MHz,CDCl₃) δ 0.83(3H,d,J=6 Hz), 1.53(3H,s), 1.56, 1.60, 1.68(each 3H,bs), 2.03, 2.06(each 3H,s), 5.0-5.3(3H,m).
Hydrolysis of acetyldictyol C (16) to dictyol C (13). An excess KOH-MeOH solution was added to a solution of 16 (12.2 mg) in MeOH. The reaction mixture was refluxed for 3 hr. The solution was diluted with water and extracted with ethyl acetate. The organic layer was washed with brine and evaporated to give an oily material (10 mg), which was identified with dictyol C (13).

Conversion of acetyldictyolal (24) to dictyolactone (22). To a solution of 24 (3.3 mg) in MeOH (0.4 ml) was added 4.9 mg of Na₂CO₃, and the reaction mixture was stirred for 48 hr at r.t. The solution was evaporated, extracted with CH₂Cl₂, and again evaporated to give oily materials. There were two new spots besides that of the starting material on TLC.

The mixture was dissolved in CH₂Cl₂ (0.5 ml), and a small amount of active MnO₂ was added. The reaction mixture was stirred for 24 hr at r.t.. After the solid residue was filtered off, the solvent was removed in vacuo, and the mixture was purified by HPLC to obtain a product identical with dictyolactone (22).

Reduction of neodictyolactone (27) to the diol 29. To a solution of 27 (10 mg) in ether (5 ml) was added 10 mg of LiAlH₄, and the reaction mixture was refluxed for 2 hr. The reaction was quenched by careful dropwise addition of water. The mixture was partitioned between ether and H₂O, and the
ether layer was washed with brine, dried over MgSO₄, and concentrated. Purification by chromatography on silica gel yielded the diol 29 (3.8 mg): C₂₀H₃₄O₂, MS m/e 306(M⁺), 288, 275, 270, 257, 149, 109, 69(base); ¹H-NMR(90 MHz,CDCl₃) δ 0.96(3H,d,J=6 Hz), 1.36, 1.56, 1.66(each 3H,bs), 4.00, 4.22(each 1H,d,J=11 Hz), 4.12(2H,s), 5.1(2H,m).

**Oxidation of the diol 29.** A solution of 29 (3.8 mg) in CH₂Cl₂ (0.5 ml) was added to a solution of sodium acetate (0.5 mg) and 2 equivalents of pyridinium chlorochromate (5.7 mg) in CH₂Cl₂ (0.2 ml). The resultant brown solution was stirred at r.t. for 2 hr. The reaction was quenched by the addition of EtOH and the mixture was partitioned between ether and H₂O. The ether layer was washed with brine, dried over MgSO₄, and evaporated to give a mixture. Purification by preparative TLC gave dictyofuran T (30) as a major product and the lactone 28: C₂₀H₃₀O₂, MS m/e 302(M⁺), 221, 191, 149, 109, 82(base), 69; ¹H-NMR spectrum is essentially the same as that of neodictyolactone (27).

**Hydrolysis of isodictyoacetal (33) to isodictyohemiacetal (23).** To a solution of 33 in dioxane-H₂O was added a small amount of p-TsOH. The reaction mixture was allowed to stand at r.t. for 3 days. The aqueous solution was extracted with ethyl acetate, and the organic layer was evaporated to give the hemiacetal, identical with isodictyohemiacetal (23).
Reaction of dictyotalide B (36). To a solution of \( \text{36} \) (0.9 mg) in dioxane (0.25 ml) was added one drop of 1N NaOH, and the mixture was allowed to stand at r.t. for 4 hr. The solution was neutralized with HCl, and extracted with ether. The ether layer was dried over MgSO\(_4\) and evaporated to give a crude products. Separation by preparative TLC yielded the compound \( \text{a} \) (44) as a major product, and the compound \( \text{b} \). \( \text{a} \) (44): \( \text{C}_{20}\text{H}_{30}\text{O}_3 \), MS m/e 318(\( \text{M}^+ \)), 300, 250, 232, 217, 140, 109, 82, 69(base); \(^{1} \text{H}-\text{NMR}(500 \text{ MHz},\text{CDCl}_3) \delta \text{0.99(3H,d,} J=6 \text{ Hz)}, \text{1.42, 1.62(each 3H,bs)}, \text{1.5(3H,bs,overlapped with H}_2\text{O signal)}, \text{3.98(1H,bs)}, \text{4.68, 4.73(each 1H,d,} J=17 \text{ Hz)}, \text{4.94(1H,dt,} J=7 \text{ Hz)}, \text{5.12(1H,ddd,} J=12, \text{4 Hz)}. \text{b: Mass spectrum is almost identical with that of} \text{a}.

Acetylation of \( \text{a} \) (44) with \( \text{Ac}_2\text{O}-\text{pyridine at r.t. did not occur.} \text{b was acetylated to give the acetate, the TLC and GC-MS of which were identical with those of} \text{36}.

Hydrogenation of acetylcoriacenone (45) and isoacetylcoriacenone (46) to 48. A 2.3 mg portion of \( \text{45} \) (46; 2.0 mg) was dissolved in EtOH, and the solution was stirred with a catalytic amount of Pd-C in a \( \text{H}_2 \) atmosphere for 8 hr. The reaction mixture was filtered and concentrated. This product is a mixture of stereoisomers, because it shows two intense spots, the Rf values of which are very close, on TLC. 48: \( \text{C}_{26}\text{H}_{36}\text{O}, \text{MS m/e 292(} \text{M}^+ \text{)}, 250, 179, 137, 109, 95(base), \text{81, 69; IR(CCl}_4) \text{1770 cm}^{-1} \).
Autoxidation of acetylcoriacenone (45) and isoacetylcoriacenone (46). A solution of 33 (17 mg) in CDCl₃ (0.3 ml) was allowed to stand in a refrigerator for 48 hr. Separation of the product by flash chromatography yielded unchanged 45 (14 mg) and the epoxide 49 (2 mg): C₂₂H₃₂O₄, MS m/e 360(M⁺), 332, 318, 300, 243, 161, 109(base), 69, 43; IR(CCl₄) 1765, 1740, 1620, 1220 cm⁻¹. Isoacetylcoriacenone was autoxidized in a similar way to give 50: C₂₂H₃₂O₄, mass and IR spectra are almost identical with those of 49; ¹H-NMR(400 MHz,CDCl₃) δ 0.96(3H,d,J=6 Hz,17-H), 1.00(3H,s,20-H), 1.58, 1.68(each 3H,bs,16,15-H), 2.11(3H,s,Ac), 2.62(1H,td,J=13, 4 Hz,3-Hₐ), 2.75(1H,dt,J=13, 4 Hz,3-Hₐ), 2.88(1H,bd,J=11 Hz,5-H), 5.07(1H,bt,J=7 Hz,13-H), 5.93(1H,s,19-H).

Cyclization of dictyodiacetal (62). To a solution of 62 (8.7 mg) in CH₂Cl₂ was added a 1% BF₃OEt₂ solution (0.3 ml) in CH₂Cl₂, and the reaction mixture was stirred for 30 min at r.t.. The reaction was quenched with H₂O, and the aqueous solution was extracted with CH₂Cl₂. The organic layer was washed with brine, dried over MgSO₄, and concentrated. Separation by preparative TLC gave 64 (1.9 mg), 65 (0.5 mg), and 66 (0.3 mg).
REFERENCES


12) B. Danise, L. Minale, R. Riccio, V. Amico, G. Oriente, M.
Platelli, C. Tringali, E. Fattorusso, S. Magno, and L.
Mayol, Experientia, 33, 413 (1977).
13) N. Enoki, K. Tsuzuki, S. Omura, R. Ishida, and T.
14) E. Fattorusso, S. Magno, L. Mayol, C. Santacroce, D. Sica,
V. Amico, G. Oriente, M. Platelli, and C. Tringali, J. C.
15) D. H. R. Batson, Rodd's Chemistry of Carbon Compounds, 1st
16) D. J. Vanderah, P. A. Steudler, L. S. Ciereszko, F. J.
Schmitz, J. D. Extrand, and D. VanderHelm, J. Am. Chem.
17) J. Finer, J. Clardy, W. Fenical, L. Minale, R. Riccio, J.
Battaile, M. Kirkup, and R. E. Moore, J. Org. Chem., 44,
2044 (1979).
(1983).
(1983).
20) M. Ishitsuka, T. Kusumi, J. Tanaka, M. Chihara, and H.
21) M. Ishitsuka, T. Kusumi, H. Kakisawa, Y. Kawakami, Y.
22) N. Enoki, H. Shirahama, E. Osawa, S. Urano, R. Ishida, and
compound 27
3-acetoxy-acetyldilophol (2)
dictyol E (14)
isopachydictyol A (18)
acetyldictyocal (24)
neodictyolactone

(27)
acetylcoriacencone
(45)
isoacetyl-coriacenone
(46)
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