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METHYL BRTAREOLATE, THE FIRST BRIAREIN DITERPENE CONTAINING A C-19 METHYL ESTER

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Abstract: The structure **1** was elucidated by 2D NMR and X-ray crystal-structure analysis, which also established the relative stereochemistry. This is the first briarein direipene containing a C-19 methyl ester.

Gorgonian octocorals of the genus *Briareum* have yielded a vast array of diterpenes possessing the briarein skeleton.'" *Briareum asbestinum* is the most widely studied of these organisms, and collections made from different geographical locations generally yield diffcrent metabolites.[1,2,7] In a continuing investigation of Caribbean marine organisms,* extracts of *Briareum asbestinum* collected off the coast of Tobago,' have afforded a new compound designated methyl briareolate, to which we have assigned structure **1** (Figure 1).

Methyl briareolate, **1**, was obtained as colourless crystals, mp 165-167 °C, $C_{31}H_{46}O_9$ (hreims 562.3112), $[\alpha]_D$ + 130.9 ° (c 0.11, CHCI,), with an ir (CHCI,) absorption at *1730* cm^{-1} (ester). The ^1H nmr spectrum had signals due to two tertiary (6 1.37, 15-H, and 1.33, 16-H_3), two secondary

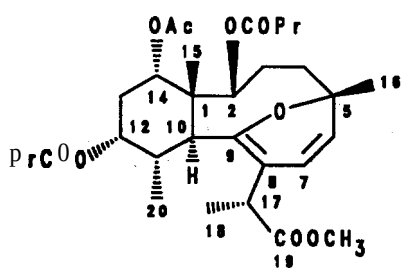

Figure 1. Structure of Methyl Briareolate.

Table 1. NMR Characteristics of Methyl Briareolate 1.[a]

Position	δ_C	δ_H (J_{HH}/Hz)	Obsd. 2- or 3- bond connectivity[b]
1.	45.71	-	3.64, 1.37
2.	77.96	4.94 (10.0)	1.37
3.	28.65	2.06, 1.39	
4.	34.88	2.20, 1.32	1.33
5.	75.14	-	5.93, 5.58, 1.33
6.	129.81	5.58 (9.3)	1.33
7.	120.15	5.93 (9.3)	3.71
a	117.33	-	5.58, 3.71, 3.64, 1.32
9.	150.95		5.93, 3.71, 3.64
10.	37.42	3.64 (11.7)	5.11, 1.37, 3.64
11.	31.84	2.21	3.64, 0.83
12.	72.07	5.11 (<3.0)	4.89, 3.64, 0.83
13.	31.23	2.08, 2.08	
14.	74.03	4.89 (3.3)	5.11, 1.37
15.	15.06	1.37	4.94, 3.64
16.	23.75	1.33	2.20
17.	37.72	3.71 (7.0)	1.32
18.	14.51	1.32 (7.0)	3.71
19.	174.30	-	3.83, 3.71, 1.32
20.	15.24	0.83 (7.0)	3.64, 2.21
C-2 butyrate			
1.	172.26		2.15
2.	36.46	2.15, 2.15 (7.3, 1.1)	0.91
3.	18.36	1.55, 1.55	2.15, 0.91
4.	13.85	0.91 (7.4)	
C-12 butyrate			
1.	172.33		2.26
2.	36.82	2.26, 2.26 (7.4, 1.5)	0.95
3.	18.61	1.66, 1.66 (7.4, 1.3)	2.26, 0.95
4.	13.95	0.95 (7.4)	
Acetate			
1.	169.77		1.92
2.	21.08	1.92	
OCH_3	51.98	3.83	

'Chemical shifts were measured at 100.6 MHz (^{13}C) and 400 MHz (^1H) for $CDCl_3$ solutions with tetramethylsilane as internal standard. [b]Obtained with FLOCK sequence."

(δ 1.32, 18-H_3 and 0.83, 20-H_3), and two primary methyl groups (δ 0.95 and 0.91). Three oxymethine protons had signals at δ 4.94, 5.11, and 4.89, and were assigned to H-2, H-12 and H-14, respectively, on the basis of a COSY experiment.

One-bond and n-bond ($n = 2,3$) connectivities were determined by 2D nmr methods, our FLOCK pulse sequence" was used to determine n-bond comrectivities. An analysis of the 2D spectra indicated that **1** was a briarein diterpene containing one acetate, two butyrates, a methyl ester, and a diene system possessing an enol ether. These results (Table 1) allowed us to determine the basic structure of the molecule. However, the attachment of the enol ether remained ambiguous. To solve this problem, a crystal was subjected to an X-ray crystal-structure analysis, which established the structure and relative stereochemistry as **1** (Figure 2).[11] Although over one hundred briarein diterpenes have been isolated to date,[2] methyl briareolate is the first one in which the lactone between C-19 and C-7 have been replaced by a methyl ester.'

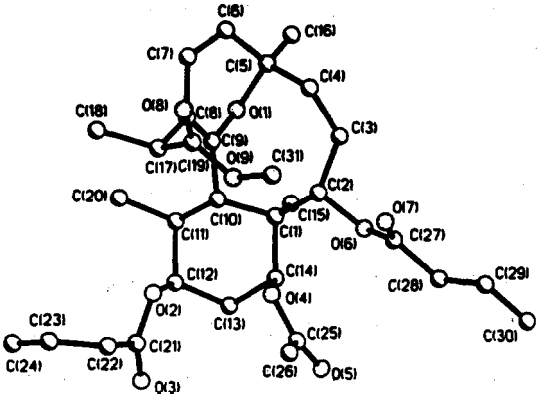

Figure 2. **ORTEP Drawing of Methyl Briareolate.**

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9. Collections and identifications were made by Mr. Richard S. Laydoo, Institute of Marine Affairs, Trinidad and Tobago. The sample was collected in South-West Tobago and was immediately stored in acetone. The acetone extract was chromatographed on silica gel using hexane-EtOAc as eluent to give methyl briareolate as colourless crystals.
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11. Colourless crystal, monoclinic, $P2_1$, $a = 9.922(1)$, $b = 9.703(2)$, $c = 17.036(2)$ Å, $\beta = 102.09(1)°$, $V = 1603.7(4)$ Å^3, $D_c = 1.165$ mg m^{-3} for Z = 2. A total of 2306 reflections ($2 < 28 < 45°$) were measured using graphite monochromated Mo $K\alpha$ radiation with variable speed o-28 scans: 2231 unique reflections ($R_{int} = 17.15\%$) and 1669 observed reflections with $I > 6\sigma(I)$ were used in the structure solution and refinement. Data were corrected for Lorentz and polarization effects but not for absorption. The structure was solved by direct methods. Refinement was by full-matrix least-squares calculations, with isotropic thermal parameters for C atoms and anisotropic thermal parameters for 0 atoms. Refinement including 361 parameters converged to give $R = 4.82\%$ and $wR = 6.60\%$ with weights (w) = $1/(\sigma^2(F_o) + 0.0027\ (F_o)^2$. Maximum electron density in the final difference map was in the range -0.18 to 0.20 e/Å^3. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.

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