



CRYSTAL STRUCTURE OF THE BRIAREIN DITERPENOID: (1S*, 2S*, 5Z, 7S*, 8R*, 9S*, 10S*, 11Z, 14S*, 17R*)- 2,14-DIACETOXY-8,17-EPOXY-9-HYDROXYBRIARA-5,11-DIEN-18-ONE

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Abstract

The crystal structure of a briarein diterpenoid, (1S*, 2S*, 5Z, 7S*, 8R*, 9S*, 10S*, 11Z, 14S*, 17R*) -2,14-diacetoxy-8,17-epoxy-9-hydroxybriara-5,11-dien-18-one isolated from a Formosan Gorgonian *Briarium* sp., has been determined by X-ray crystallographic method. The molecule crystallized in orthorhombic group $P2_12_12_1$, with cell dimension $a = 8.805(2)$, $b = 14.125(3)$, $c = 18.299$ Å. The final R and R_w values for 1319 observed reflections are 0.043 and 0.056, respectively. The molecule has fused 6- and 10 membered rings, a γ -lactone ring, two acetates, and two trisubstituted double bonds. The relative configuration has been fully determined.

1. Introduction

Gorgonians (order Gorgonacea) and soft coral (Alcyonacea) are known to be important sources of diterpenoids in marine environment. The genus *Briareum* has been found to be situated near the transition between the Gorgonacea and Alcyonacea. A large number of briarein diterpenes have been isolated from the Gorgonacean genus *Briareum* [1, 2] and the Alcyonacean genus *Minabea* [3], as well as in sea pancy and sea pens [4, 5]. Several briareins have been found to show interesting biological activities, such as antifouling activity [6] and cytotoxic activity [7]. As part of our studies directed in searching bioactive compounds from marine organisms of southern Taiwan, an investigation of the secondary metabolites from Taiwan soft coral *Briareum* sp. has been carried out and has led to the isolation of a known briarein diterpenes, (1S*, 2S*, 5Z, 7S*, 8R*, 9S*, 10S*, 11Z, 14S*, 17R*)-2, 14-diacetoxy -8,17 -epoxy -9 -hydroxybriara-5,11-dien-18-one (1) [8]. Herein, the 3-dimensional crystal structure of this compound has been determined and reported.

2. Sample preparation and isolation procedure

The ethyl acetate extract from the organism of Briarein species, collected at Keng-Ting, Taiwan, in 1991 by SCUBA diving, was chromatographed on a silica gel column (hexane/ethyl acetate, 1:3) yielding the product (1) as colourless prisms (the single crystal for X-ray diffraction analysis was obtained by slow evaporation of ethyl acetate solution): mp 239-241 °C; $[\alpha]_D + 13^\circ(\text{C } 0.32, \text{CHCl}_3)$. ¹H-NMR and ¹³C-NMR spectra of (1) [8] reveal that this

molecule is the 9-deacetyl derivative of briareolide H, a compound has been reported previously [5].

3. Data collection from X-ray diffractometer

Preliminary examination and diffraction data collection for the single crystal were performed with MoK α radiation ($\lambda = 0.71073$ Å) on a CAD4 Kapa geometry four-circle X-ray diffractometer. A single crystal can be rotated to any position on the diffractometer controlled by PC, with the orientation matrix determined. The diffractometer is equipped with an incident beam graphite monochromator. Cell constants and orientation matrix for data collection were obtained from least-squares refinement, using the setting angle of 25 reflections in the range, $12^\circ \leq 2\theta \leq 25^\circ$, measured by computer controlled diagonal slit method of centering. The orthorhombic cell parameters and calculated volume are: $a = 8.805(2)$ Å, $b = 14.125(3)$ Å, $c = 18.299(4)$ Å, $V = 2275.8(11)$ Å³. For $Z = 4$ and $FW = 448.5$, the calculated density is 1.309 g/cm³. As a check on crystal quality, ω -scan profiles of several intense reflections were plotted; the half-width was about 0.15 degree, with the take off angle of 2.8°, indicating good crystal quality. From the systematic absence ($h00$, h odd; $0k0$, k odd; $00l$, l odd) and from the subsequent least-squares refinement, the space group $P2_12_12_1$ was determined.

The data were collected at a room temperature using $\omega/2\theta$ scan technique. The scan speed varied from 2 to 29.3 °/min (in ω). The variable scan speed allows rapid data collection for intense reflections where a fast scan rate is used and assures good counting statistics for weak reflections where a slow scan speed is used. Data were collected to a maximum of 45° (2θ). The scan range was determined as a function of θ to correct for the separation of the K α doublet. The scan width was calculated as follows: ω -scan width = $0.7 + 0.350 \tan \theta$ (in degrees). Background was measured with the crystal and counter fixed at the beginning and end of the scan, each for 50% of the total scan time. The counter aperture was also adjusted as a function of θ . The horizontal aperture width ranged from 1.5 to 2.2 mm; the vertical aperture was set at 4.0 mm. IBM personal computer connected to "NaI (Tl activated) scintillation counter coupled to a single channel analyser" was used for the diffracted X-ray data collection. Dead time correction was applied for counting rate larger than 100000 counts/sec.

4. Data reduction

The data reduction was performed using the SDP program package [9]. A total of 1957 reflections were collected (1721 unique and 1319 reflections with $F_o > 4\sigma(F_o)$ were regarded as observed). As a check of crystal and electric stability, 3 representative reflections were measured every 60 min. The fluctuation of the average intensity for the 3 check reflections is around 1 %. Hence, a linear time decaying correction was applied. The correction factors on intensities ranged from 1.00 to 1.003 with an average value of 1.015.

Lorentz and polarization corrections were applied to the data. The linear absorption coefficient is 0.098 mm^{-1} for $\text{MoK}\alpha$ radiation. An empirical absorption correction based on a series of ψ -scans was applied to the data. Relative transmission coefficients ranged from 94.0 to 98.0 with an average value of 96.0.

5. Structure solution and refinement

The structure was solved using direct methods as incorporated in SHELXS [10]. The remaining atoms were located in succeeding difference Fourier syntheses. The structure was refined in full matrix least-squares calculation, the function minimized was $\sum w(|F_c| - |F_o|)^2$; where the weighting factor w has the form, $w^{-1} = \sigma^2(F_o) + 0.0013F_o^2$. The standard deviation on intensities, $\sigma(F_o^2)$ is defined as follows,

$$\sigma(F_o^2) = \{ [S^2(C + R^2B) + (pF_o^2)^2] / Lp^2 \}^{1/2}$$

where S is the scan rate, C is the total integrated peak count, R is the ratio of scan time to background counting time, B is the total background count, Lp is the Lorentz-polarization factor, and p is a factor introduced to downweight intense reflections. Here, p was set to 0.04.

Scattering factors were taken from Cromer and Weber [11]. Anomalous dispersion effects were included in F_c [12]; the values for dispersion correction factors $\Delta f'$ and $\Delta f''$ were those of Cromer [12]. Only the reflections having intensities larger than three times their standard deviation were used in the refinements. The final refinement include 323 variable parameters and converged with unweighted and weighted agreement factors of:

$$R = \frac{\sum |F_c| - |F_o|}{\sum |F_o|} = 0.043$$

$$R_w = \left(\frac{\sum w(|F_c| - |F_o|)^2}{\sum wF_o^2} \right)^{1/2} = 0.056$$

Goodness of fit is 1.27. The highest peak in the final difference Fourier had a height of $0.20 \text{ e}/\text{\AA}^3$ and largest difference hole of $-0.15 \text{ e}/\text{\AA}^3$ with an estimated error based on ΔF of 0.05. Crystallographic parameters, experimental intensity measurements and details of the crystal data, structure solution and refinement are listed in Tables 1-3, respectively. All the calculations were performed on a personal

computer (with Intel 586 CPU). SDP program package was used in data reduction and the structure was solved by direct methods incorporated in SHELXSTM software packages.

6. Result and discussion

Atomic coordinates and equivalent isotropic displacement coefficients $U(eq)$, bond angles and bond lengths are normal (Table 1). The F-tables can be obtained from the first author. As shown in Fig. 1, the structure determined by X-ray diffraction showed that the compound possesses a half-chair conformation for the six-member ring. It also reveals the existence of a 10-membered ring which is in twisted chair form and is trans ring fused with both the 6-membered ring at C(1) and C(10) and the γ -lactone ring at C(7) and C(8). All of the four bonds fusing the 10-membered ring to both the 5- and 6-member rings are oriented nearly equatorially with respect to the latter two rings. The endocyclic double bonds of 6- and 10-membered rings are in cis configuration. The C(2) and C(14) acetate groups are placed in equatorial orientation. The C(17) methyl group of the γ -lactone ring is placed in equatorial orientation. An epoxide was formed at C(8) and C(17). Two trisubstituted double bonds are located at C(5), C(6) and C(11), C(12) respectively.

Crystal Data

Empirical Formula	$\text{C}_{24}\text{H}_{32}\text{O}_8$
Color; Habit	Colorless, plate like
Crystal size(mm)	$0.25 \times 0.19 \times 0.44$
Crystal system	Orthorhombic
Space group	$P2_12_12_1$
Cell dimensions	$a = 8.805(2) \text{ \AA}$ $b = 14.125(3) \text{ \AA}$ $c = 18.299(9) \text{ \AA}$
volume	$2275.9(9) \text{ \AA}^3$
Z	4
Mr (Formula weight)	448.5
Density(calc.)	1.309 g/cm^3
X-ray wave length	0.71073 \AA (MoK α)
Absorption Coefficient	0.098 mm^{-1}
F(000)	960

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Solution and refinement

System Used	Siemens SHELXTL PLUS
Solution	Direct Methods
Refinement Method	Full-Matrix Least-Squares
Quantity minimized	$\sum w(F_o - F_c)^2$
Absolute Structure	$\eta = 4(6)$
Extinction Correction	$\chi = 0.0034(9)$, where $F^* = F [1 + 0.002\chi F^2 / \sin(2\theta)]^{-1/4}$
Hydrogen Atoms	Riding model, fixed isotropic U
Weighting Scheme	$w^{-1} = \sigma^2(F) + 0.0013F^2$
Number of Parameter Refined	323
Final R Indices (obs. data)	$R = 4.30\%$, $wR = 5.62\%$
R Indices (all data)	$R = 6.43\%$, $wR = 6.80\%$
Goodness-of-Fit	1.27
Largest and Mean Δ/σ	0.211, 0.009

Table 1. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement coefficients ($\text{\AA}^2 \times 10^3$)

	x	y	z	U(eq)
O(1)	1626(5)	6801(3)	3894(2)	53(1)
O(2)	-879(6)	6990(4)	3742(3)	89(2)
O(3)	248(5)	3996(5)	6823(2)	61(2)
O(4)	741(5)	2675(4)	7458(2)	81(2)
O(5)	435(4)	2884(3)	5600(2)	52(1)
O(6)	3769(4)	4459(3)	5424(2)	50(1)
O(7)	527(4)	5031(2)	3080(2)	42(1)
O(8)	648(6)	5812(3)	2016(2)	69(2)
C(1)	2450(6)	5160(4)	4020(3)	40(2)
C(2)	1426(6)	5941(3)	4342(3)	39(2)
C(3)	1688(7)	6222(4)	5135(3)	49(2)
C(4)	247(7)	6461(4)	5555(3)	56(2)
C(5)	-932(8)	5691(4)	5531(3)	48(2)
C(6)	-686(7)	4809(4)	5775(3)	51(2)
C(7)	701(6)	4430(4)	6128(3)	47(2)
C(8)	1504(6)	3654(4)	5705(3)	43(2)
C(9)	2679(6)	3834(4)	5124(3)	39(2)
C(10)	1978(5)	4178(3)	4360(3)	37(2)
C(11)	2138(6)	3346(4)	3819(3)	42(2)
C(12)	2626(7)	3430(4)	3148(3)	53(2)
C(13)	2975(8)	4352(4)	2794(3)	59(2)
C(14)	2165(6)	5141(4)	3190(3)	46(2)
C(15)	4158(7)	5422(5)	4098(3)	57(2)
C(16)	-2425(8)	5930(6)	5168(4)	76(3)
C(17)	1548(6)	2824(4)	6193(3)	51(2)
C(18)	2564(9)	1982(5)	6179(4)	70(3)
C(19)	821(7)	3116(5)	6891(3)	59(2)
C(20)	1637(8)	2382(4)	4075(3)	55(2)
C(21)	400(10)	7238(4)	3630(3)	60(2)
C(22)	828(11)	8087(5)	3191(4)	82(3)
C(23)	-91(7)	5422(4)	2490(3)	49(2)
C(24)	-1795(8)	5359(5)	2495(4)	68(2)

Table 2. Bond lengths (Å)			
C(1)-C(2)	1.542(7)	C(1)-C(10)	1.575(7)
C(1)-C(14)	1.541(7)	C(1)-C(15)	1.556(8)
C(2)-C(3)	1.523(7)	C(2)-O(1)	1.475(6)
C(3)-C(4)	1.521(9)	C(4)-C(5)	1.500(8)
C(5)-C(6)	1.332(8)	C(5)-C(16)	1.525(10)
C(6)-C(7)	1.482(8)	C(7)-C(8)	1.518(8)
C(7)-O(3)	1.467(7)	C(8)-C(9)	1.505(7)
C(8)-C(17)	1.474(8)	C(8)-O(5)	1.450(6)
C(9)-C(10)	1.604(7)	C(9)-O(6)	1.415(6)
C(10)-C(11)	1.543(7)	C(11)-C(12)	1.306(8)
C(11)-C(20)	1.507(8)	C(12)-C(13)	1.486(8)
C(13)-C(14)	1.509(8)	C(14)-O(7)	1.465(6)
C(17)-C(18)	1.488(9)	C(17)-C(19)	1.487(8)
C(17)-O(5)	1.465(7)	C(19)-O(3)	1.348(9)
C(19)-O(4)	1.211(8)	C(21)-C(22)	1.493(10)
C(21)-O(1)	1.334(9)	C(21)-O(2)	1.197(10)
C(23)-C(24)	1.503(10)	C(23)-O(7)	1.329(7)
C(23)-O(8)	1.215(8)		

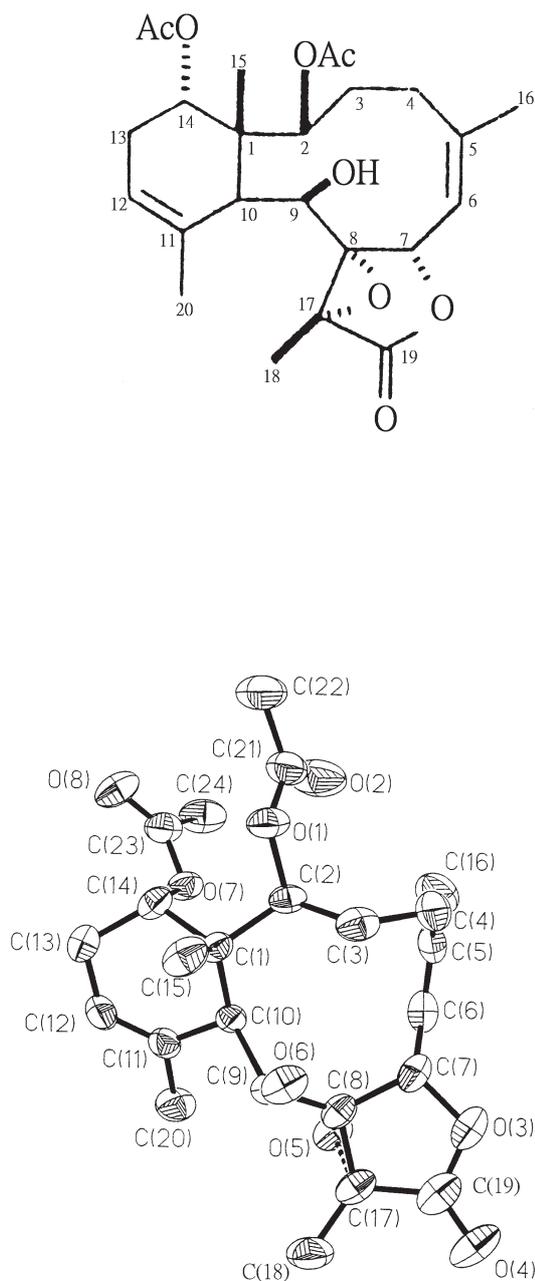


Fig. 1. Chemical structural diagram (top) and ORTEP plot (bottom) of the molecule



C(1)-C(2)-C(3)	117.5(4)	C(1)-C(2)-O(1)	107.9(4)
C(1)-C(10)-C(9)	120.6(4)	C(1)-C(10)-C(11)	113.1(4)
C(1)-C(14)-C(13)	114.1(5)	C(1)-C(14)-O(7)	107.3(4)
C(2)-C(1)-C(10)	109.0(4)	C(2)-C(1)-C(14)	107.0(4)
C(2)-C(1)-C(15)	111.1(4)	C(2)-C(3)-C(4)	114.4(5)
C(2)-O(1)-C(21)	119.0(5)	C(3)-C(2)-O(1)	107.3(4)
C(3)-C(4)-C(5)	113.3(5)	C(4)-C(5)-C(6)	124.4(5)
C(4)-C(5)-C(16)	116.3(5)	C(5)-C(6)-C(7)	127.4(6)
C(6)-C(5)-C(16)	119.2(6)	C(6)-C(7)-O(3)	107.8(4)
C(7)-C(8)-C(9)	123.9(5)	C(7)-C(8)-C(17)	106.1(4)
C(7)-C(17)-O(5)	107.9(4)	C(7)-O(3)-C(19)	111.3(4)
C(8)-C(7)-C(6)	115.0(4)	C(8)-C(7)-O(3)	105.5(4)
C(8)-C(9)-C(10)	113.7(4)	C(8)-C(9)-O(6)	107.3(4)
C(8)-C(17)-C(18)	129.8(5)	C(8)-C(17)-C(19)	106.8(5)
C(8)-C(17)-O(5)	59.1(3)	C(8)-O(5)-C(17)	60.8(3)
C(9)-C(8)-C(17)	123.0(5)	C(9)-C(8)-O(5)	118.7(4)
C(9)-C(10)-C(11)	107.1(4)	C(10)-C(1)-C(14)	109.3(4)
C(10)-C(1)-C(15)	115.4(4)	C(10)-C(9)-O(6)	114.3(4)
C(10)-C(11)-C(12)	124.4(5)	C(10)-C(11)-C(20)	117.5(4)
C(11)-C(12)-C(13)	123.8(5)	C(12)-C(11)-C(20)	118.1(4)
C(12)-C(13)-C(14)	109.9(5)	C(13)-C(14)-O(7)	108.7(5)
C(14)-C(1)-C(15)	104.6(4)	C(14)-O(7)-C(23)	118.0(4)
C(17)-C(8)-O(5)	60.1(3)	C(17)-C(19)-O(3)	109.7(5)
C(17)-C(19)-O(4)	128.1(7)	C(18)-C(17)-C(19)	119.7(5)
C(18)-C(17)-O(5)	115.8(5)	C(19)-C(17)-O(5)	109.4(5)
C(22)-C(21)-O(1)	111.3(7)	C(22)-C(21)-O(2)	124.4(7)
C(24)-C(23)-O(7)	112.2(5)	C(24)-C(23)-O(8)	124.4(6)