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X-RAY CRYSTAL STRUCTURE OF 3,4-EPOXYPALISADIN A

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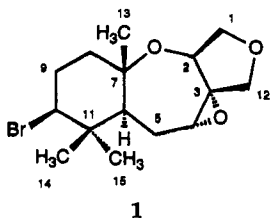
ABSTRACT.—The structure of 3,4-epoxypalisadin A (**1**), isolated from the marine red alga *Laurencia flexilis*, has been confirmed by X-ray crystallographic analysis. The results of this analysis also enabled the stereochemistry of the 3,4-epoxy function to be determined as 3 α and 4 α , and the absolute configuration of all chiral centers to be determined. Within the crystal of **1**, two independent molecules were shown to exist, differing primarily in the conformation of the five-membered ring.

Recently we isolated a series of new sesquiterpenes from the marine red alga *Laurencia flexilis* (**1**). In that report the stereochemistry for the 3,4-epoxy function of 3,4-epoxypalisadin A (**1**) was not given because it could not be assigned unambiguously. More recently, we have been able to produce a suitable crystal of **1**, and, in this communication, its X-ray crystal structure determination is reported.

As the stereochemistry of the 3,4-epoxy function of **1** could not be resolved unambiguously from the results of extensive ¹H-nmr studies, an X-ray crystallographic analysis of **1** was deemed necessary. Compound **1**, a clear, crystalline compound, mp 119–122° yielded a single large crystal suitable for X-ray crystallographic analysis. The structure was initially solved at 22° with data collected in CuK α radiation, using a fragment of this crystal sealed in a capillary. The crystal underwent rapid, anisotropic intensity decay amounting to 52% during data

collection, and the crystal turned brown during the experiment. While correction for the decay was reasonably successful, and a final R value of 0.075 was achieved, the precision was somewhat limited, and the absolute configuration could not be unambiguously determined. In order to prevent the severe decay, increase the precision, and determine the absolute configuration, we recollected the data with MoK α radiation at 115K, using another fragment of the same large crystal.

The results of the study confirmed all previous deductions concerning the structure of **1**, and additionally established the 3,4-epoxy function to have the alpha configuration, and the chiral centers to have the absolute configuration shown in Figure 1. Within the structure all bond lengths and angles are considered average for the particular bond type, with all C(sp³)-C(sp³) lengths being in the range 1.444(5)–1.545(4) Å, and C(sp³)-O ether distances being between 1.411(4) and 1.468(4) Å. The C(sp³)-Br bond lengths of 1.978(3) Å and 1.988(9) Å were also considered unexceptional. A major point of interest derived from this study was the fact that two independent molecules, **1A** and **1B**, exist in the crystal; see Figure 1. Their conformations are very similar, with the exception of the position of O-2. In both, the six-membered ring exists in the chair conformation with endocyclic torsion angle magnitudes ranging from



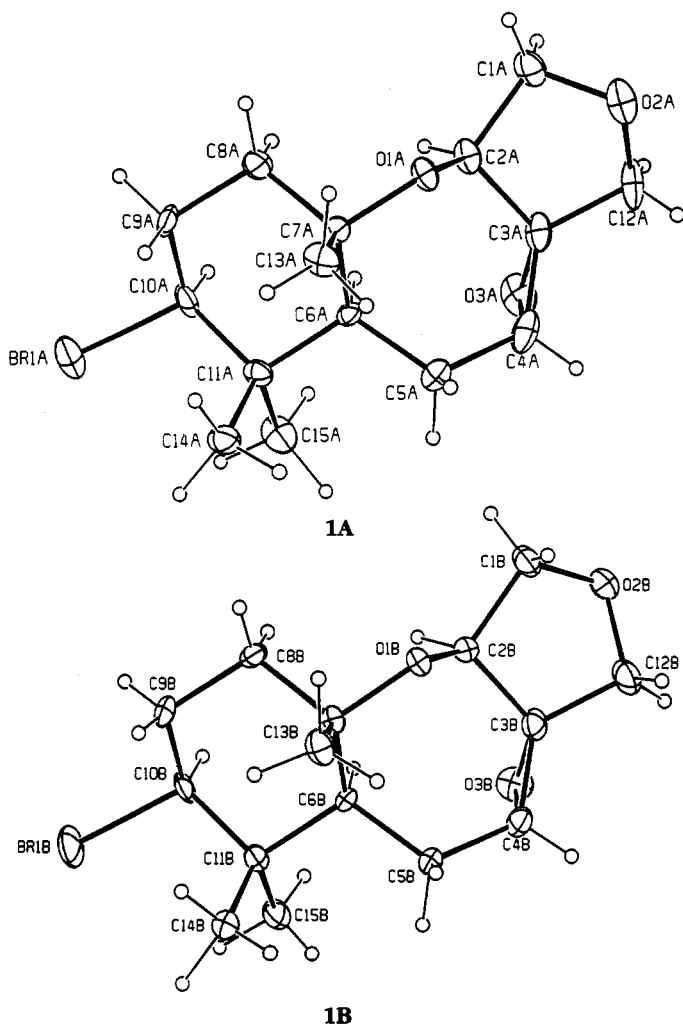


FIGURE 1. ORTEP drawings of 1A and 1B at 115 K, with 50% ellipsoids. H atoms are represented by circles of arbitrary radius.

52.3(3)° to 60.1(4)°. In both, the seven-membered ring exists in a twist conformation having the two-fold twist axis passing through C-7 and the midpoint of the C-3-C-4 bond. In both, the five-membered ring has the envelope conformation with ether oxygen atom O-2 at the flap position. In the **A** molecule, the orientation of the flap O-2 is beta, while in the **B** molecule, it is alpha-oriented.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Compound **1** was recrystallized from hexane. Remaining details as previously described (1).

X-RAY DATA FOR 1.—The unit-cell dimensions at room temperature (22°) are $a=9.7152(9)$, $b=7.2426(4)$, $c=21.456(2)$ Å, $\beta=97.020(7)^\circ$, $V=1498.4(4)$ Å³. These were determined on an Enraf-Nonius CAD4 diffractometer using CuK α radiation, and a crystal fragment sealed in a capillary. The structure was solved using data collected from this fragment to $\theta=75^\circ$, and refined to $R=0.075$ over 2317 observed data. A second fragment of the same crystal was used to collect the 115 K data with MoK α radiation on another CAD4 diffractometer. An Enraf-Nonius N₂ gas stream cryostat was used to cool the sample. Cell dimensions at 115 K (Table 1) were determined by least-squares refinement using the angular positions of 25 reflections in the 2θ range 20–26°. One quadrant of data was collected to a maximum θ value of 30°, and a second quadrant, inequivalent under

TABLE 1. Crystal Structure Data for 1.

Crystal dimensions	0.50×0.55×0.58 mm
Crystal color	Colorless
Molecular formula	C ₁₅ H ₂₃ O ₅ Br
Molecular weight	331.3
<i>a</i>	9.602(4) Å
<i>b</i>	7.188(2) Å
<i>c</i>	21.279(7) Å
α	90°
β	97.55 (3)°
γ	90°
<i>V</i>	1456(2) Å ³
<i>F</i> ₀₀₀	688
μ (CuKα)	28.0 cm ⁻¹
λ (CuKα)	0.71073 Å
<i>Z</i>	4
<i>D</i> _{calc}	1.512 gcm ⁻³
θ _{range}	1–30°
Refined variables	525
Unique data	6881
Observed data	5933
<i>R</i>	0.035
<i>R</i> _w	0.035
Space group	P2 ₁ , monoclinic
Temp	115 K
Min. rel. transm	89.99%
Max. rel. transm	99.94%
Av. rel. transm	95.69%
Intensity decay	2.4%
Min. residual	–0.20 eÅ ⁻³
Max. residual	1.36 eÅ ⁻³

TABLE 2. Coordinates and Equivalent Isotropic Thermal Parameters and their Estimated Standard Deviations for 1A.

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i> _{eq} (Å ²) ^a
Br-1A	0.42591(4)	0	0.73275(2)	2.261(6)
O-1A	0.8851(2)	–0.1270(3)	0.5599(1)	1.27(4)
O-2A	0.9525(2)	–0.1942(4)	0.4252(1)	2.16(5)
O-3A	0.6177(3)	–0.3633(4)	0.4666(1)	2.32(5)
C-1A	0.8948(3)	–0.0341(5)	0.4523(1)	1.79(7)
C-2A	0.8020(3)	–0.1100(5)	0.4995(1)	1.31(6)
C-3A	0.7619(3)	–0.3012(5)	0.4724(2)	1.67(7)
C-4A	0.7249(4)	–0.4549(5)	0.5107(2)	2.14(7)
C-5A	0.7118(4)	–0.4447(5)	0.5806(2)	1.72(7)
C-6A	0.6779(3)	–0.2489(4)	0.6026(1)	1.06(6)
C-7A	0.8102(3)	–0.1253(5)	0.6154(1)	1.14(6)
C-8A	0.7675(4)	0.0733(5)	0.6277(2)	1.51(6)
C-9A	0.6767(4)	0.0825(5)	0.6816(2)	1.62(6)
C-10A	0.5491(3)	–0.0398(5)	0.6664(1)	1.54(6)
C-11A	0.5792(3)	–0.2467(4)	0.6563(1)	1.24(6)
C-12A	0.8387(4)	–0.3214(6)	0.4143(2)	2.45(8)
C-13A	0.9236(3)	–0.1923(5)	0.6671(1)	1.64(6)
C-14A	0.6422(4)	–0.3439(5)	0.7176(2)	1.61(6)
C-15A	0.4412(4)	–0.3442(6)	0.6312(2)	2.12(7)

$$^a B_{eq} = (8\pi^2/3) \sum_i U_{ij} a_i^* a_j^* a_i \cdot a_j$$

TABLE 3. Coordinates and Equivalent Isotropic Thermal Parameters and their Estimated Standard Deviations for **1B**.

Atom	x	y	z	$B_{eq}(\text{\AA}^2)^a$
Br-1B	0.94182(4)	-0.21416(7)	0.25022(2)	2.370(6)
O-1B	0.6284(2)	-0.0520(3)	-0.0161(1)	1.37(4)
O-2B	0.7558(2)	-0.0225(4)	-0.16224(9)	1.76(4)
O-3B	0.9411(2)	0.1790(4)	-0.0379(1)	2.14(5)
C-1B	0.6806(4)	-0.1244(5)	-0.1204(2)	1.65(7)
C-2B	0.7388(4)	-0.0571(5)	-0.0538(2)	1.56(6)
C-3B	0.7963(3)	0.1319(5)	-0.0663(2)	1.45(6)
C-4B	0.8228(3)	0.2775(5)	-0.0188(1)	1.53(6)
C-5B	0.7902(3)	0.2560(4)	0.0484(1)	1.42(6)
C-6B	0.7994(3)	0.0550(4)	0.0731(1)	1.05(6)
C-7B	0.6642(3)	-0.0575(4)	0.0531(1)	1.23(6)
C-8B	0.6884(3)	-0.2600(4)	0.0726(2)	1.31(6)
C-9B	0.7370(4)	-0.2773(5)	0.1436(2)	1.64(6)
C-10B	0.8705(3)	-0.1666(5)	0.1602(1)	1.48(6)
C-11B	0.8592(3)	0.0415(4)	0.1457(1)	1.31(6)
C-12B	0.7605(4)	0.1623(5)	-0.1369(2)	2.03(7)
C-13B	0.5311(3)	0.0170(5)	0.0746(1)	1.59(6)
C-14B	0.7715(4)	0.1459(5)	0.1892(2)	1.74(7)
C-15B	1.0083(4)	0.1229(5)	0.1544(2)	1.87(7)

$$^a B_{eq} = (8\pi^2/3) \sum_i \sum_j U_{ij} a_i^* a_j^* a_i a_j$$

anomalous scattering, was collected to $\theta=25^\circ$. A total of 7287 data was collected, using ω - 2θ scans with variable scan width and variable scan rate. Data were collected for background, Lorentz, polarization, and absorption effects. The absorption corrections were based on ψ scans, and relative transmission coefficients are given in Table 1. Whereas intensities had decayed by over 50% at room temperature, decay during cryogenic data collection was limited to less than 3%. After elimination of systematic absences and averaging of redundant data, 5933 of the 6881 unique data were considered observed [$I > 3\sigma(I)$] and were used in the refinement.

Coordinates from the room temperature determination were used as a beginning refinement model. The structure had originally been solved using MULTAN (2) and DIRDIF (3). Refinement was carried out by full-matrix least squares based on F_o with weights $w = \sigma^{-2}(F_o)$. The function minimized was $\sum w(F_o - |F_c|)^2$. Non-hydrogen atoms were refined anisotropically, while hydrogen atoms were refined isotropically. As a result of the small isotropic thermal parameters of the H atoms at low temperature as well as their relatively large uncertainties, the thermal parameter of one H atom tended to refine to a negative value. This parameter was fixed at a value of 1.0 \AA^2 . All calculations were carried out using the MOIEN programs (4). At convergence, $R=0.035$, $R_w=0.035$, and $GOF=1.582$. The absolute configuration was determined by refinement of the inversion-related structure under identical cir-

cumstances, yielding $R=0.067$, $R_w=0.074$, $GOF=3.355$. Thus, the configuration illustrated in Figure 1 was demonstrated to be correct. The final atomic coordinates for **1A** and **1B** are listed in Tables 2 and 3, respectively.¹

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¹Atomic coordinates for this compound have been deposited with the Cambridge Crystallographic Data Centre and can be obtained upon request from Dr. Olga Kennard, University Chemical Laboratory, 12 Union Road, Cambridge CB2 1EZ, UK.