X-Ray Structure Determination of (−)-Obtusane, a New Sesquiterpene from the Red Alga, *Laurencia nipponica* Yamada

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(Received May 12, 1983)

Synopsis. A new sesquiterpene ($C_{15}H_{23}Br_2Cl$, mp 172—173 °C) isolated from *Laurencia nipponica* Yamada has been found to be (−)-obtusane by X-ray crystal structure analysis.

In continuing studies on the constituents of the red alga, *Laurencia nipponica* Yamada, collected at Akkeshi on the Pacific Coast of Hokkaido,[1] we have isolated a new sesquiterpene hydrocarbon (**1**). The ^1H and ^{13}C NMR spectra of **1** show a close resemblance to those of obtusane (**2**) isolated from *Laurencia obtusa*,[2] while the specific rotations of **1** and **2** are equal in magnitude but opposite in sign. These facts suggest that **1** may be the enantiomer of **2**. In order to establish the molecular structure of **1**, we have now carried out an X-ray crystal structure analysis.

Experimental

Isolation. *Laurencia nipponica* Yamada collected at Akkeshi, Hokkaido, was extracted with methanol. The neutral methanol extracts (*ca.* 1% of the half-dried alga) obtained by the conventional methods were chromatographed over alumina. The fraction eluted with hexane–benzene (1:1 volume ratio) was rechromatographed over silica gel to yield **1** (0.09% of the extracts); mp 172—173 °C (from diisopropyl ether), $[\alpha]_D^{22}$ −38.5° (*c* 0.55, $CHCl_3$); IR (Nujol) ν_{max} 3100, 1640, 1222, 1198, 1158, 1092, 1058, 1028, 972, 916, 876, 800, 778, 726, 664, 642, and 624 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.96, 1.14, 1.83 (each 3H, s), 1.6—2.4 (10H, m), 4.45 (1H, dd, J=13 and 4 Hz), 4.72 (1H, dd, J=13 and 5 Hz), 4.87, and 5.26 (each 1H, s); ^{13}C NMR ($CDCl_3$, 50.1 MHz) δ 145.8 (=C〈), 114.9 (=CH_2), 68.4 (〉C〈), 68.0, 63.6 (each 〉CH–), 50.5, 44.0 (each 〉C〈), 40.5, 37.3, 35.9, 33.6, 25.7 (each –CH_2–), 24.0, 23.7, and 17.6 (each CH_3); MS *m/e* (rel intensity) 402, 400, 398, 396 (1:4:9:3, M^+), 321, 319, 317 (2:9:5, M^+−Br), 320, 318, 316 (2:9:4, M^+−HBr), 283, 281 (9:9, M^+−HBr−Cl), 239, 237 (3:18, M^+−HBr−Br), 201 (31, M^+−HBr−Br−HCl), 109 (98), 107 (22), 105 (30), 95 (66), 93 (38), 91 (30), 81 (23), 69 (100), 67 (28), 55 (19), and 41 (91). Found: *m/e* 399.9846. Calcd for $C_{15}H_{23}{}^{81}Br_2{}^{35}Cl$: M 399.9816. The melting point was uncorrected. The IR spectrum was measured on a Hitachi EPI-G2 spectrometer. The ^1H and ^{13}C NMR spectra were recorded on a JEOL FX-200 spectrophotometer, TMS being used as an internal reference. The low and high resolution mass spectra were obtained with a JEOL JMS-D300 spectrometer. The optical rotation was measured on a JASCO DIP-140 polarimeter.

X-Ray Measurement. A colorless single crystal cut into a cube with an edge of *ca.* 0.2 mm was used. The crystal data were as follows: $C_{15}H_{23}Br_2Cl$, mol wt 398.61, orthorhombic, space group $P2_12_12_1$, a=10.580(3), b=20.537(6), c=7.492(2) Å, Z=4, D_c=1.626 g cm^{-3}, μ(Mo $K\alpha$)=50.8 cm^{-1}. The cell dimensions and diffraction intensities were measured on a Rigaku four-circle diffractometer at the High Brilliance X-Ray Diffraction Laboratory of Hokkaido University, using graphite-monochromated Mo $K\alpha$ radiation (λ=0.71073 Å). The θ—2θ scanning technique was applied at a θ scan rate of 2° min^{-1}; the background was counted for 10 s at each end of the scan range. Three standard reflections, measured at intervals of every 100 reflections, showed a gradual decrease in intensity during the course of data collection; the final-intensity/initial-intensity ratios were *ca.* 0.91—0.98. The intensities were corrected for this damage to the sample as well as for the Lorentz and polarization factors, but not for the absorption or the extinction effect. In the range of 2θ values up to 50°, 1131 independent structure factors above the $3\sigma(F)$ level were selected for the structure determination.

Structure Determination

The structure was solved by the Monte Carlo direct method,[3] using the 20 reflections with the greatest $|E|$ values as the starting set. The seventhly-generated random phase set led to the correct solution; an E-map based on 499 phases revealed all the non-hydrogen atoms. After the structure had been well refined by the block-diagonal least-squares method with anisotropic temperature factors, the absolute configuration was determined by taking account of the anomalous dispersion of the halogen atoms for Mo $K\alpha$ radiation. The R ratio for the two enantiomeric structures, 1.10, excluded one of them at a 99.5% confidence level.[4] Since a difference Fourier map revealed all the hydrogen atoms, further least-squares refinements were carried out including the hydrogen atoms. For these refinements, the following weighting scheme was used:

$$w = 1/\{\sigma(F)^2 \exp(c_1X^2+c_2Y^2+c_3XY+c_4X+c_5Y)\},$$

where $X=|F_o|$ and $Y=\sin\theta/\lambda$. The c_1, c_2, c_3, c_4, and c_5 coefficients were evaluated from the $(\Delta F)^2$ distribution; $c_1=-0.208\times10^{-3}$, c_2=27.5, $c_3=-0.908\times10^{-2}$, c_4=0.0502, and $c_5=-25.0$. In this manner, the R value reached 0.050. The final atomic parameters are listed in Table 1.[5]

The calculations were done on a HITAC M-200H computer at the Hokkaido University Computing Center, using our own programs. The atomic scattering factors were taken from the International Tables.[6]

Results and Discussion

The molecular structure of **1** including the absolute configuration is shown in Fig. 1, while the bond distances and angles are given in Fig. 2. Thus, it is concluded that this new sesquiterpene is the enantiomer of obtusane,[2] *i.e.*, (−)-obtusane.

Each of the six-membered A- and B-rings has a

Table 1. The final atomic parameters and estimated standard deviations

Atom	10^4x	10^4y	10^3z	B_{eq}[a)]/Å^2
Br(1)	−3693(1)	1421.5(7)	−136.1(2)	6.07
Br(2)	3380(1)	1639.2(7)	537.8(2)	5.35
Cl	−3485(3)	284(2)	197.8(5)	5.46
C(1)	−1181(10)	757(5)	270(2)	3.34
C(2)	−2174(9)	776(5)	122(2)	3.07
C(3)	−2604(9)	1480(6)	79(2)	3.75
C(4)	−1416(11)	1847(5)	25(2)	4.32
C(5)	−466(10)	1856(4)	176(2)	3.66
C(6)	13(9)	1157(5)	226(1)	2.69
C(7)	773(9)	851(5)	76(2)	3.42
C(8)	1934(10)	1224(6)	23(2)	4.10
C(9)	2830(9)	1289(6)	183(2)	3.78
C(10)	2130(9)	1570(5)	337(2)	3.53
C(11)	944(10)	1192(5)	397(1)	3.27
C(12)	338(10)	1549(7)	555(2)	4.73
C(13)	1263(10)	492(5)	453(2)	3.68
C(14)	533(12)	272(6)	4(2)	5.13
C(15)	−3358(11)	1834(6)	218(2)	5.45

a) $B_{eq}=8\pi^2(u_1^2+u_2^2+u_3^2)/3$, where u_i is the root-mean-square deviation in the ith principal axis of the thermal ellipsoid.

chair conformation. The C(7)=C(14)H_2 and C(15)H_3 groups occupy the axial positions on the A-ring, while the Cl and Br(1) atoms and the C(11)Me_2 group take the equatorial orientations. Because of the *syn*-periplanar conformation (torsion angle, −7(2)°) of the C(1)–C(6)–C(7)=C(14) segment, the C(14)H_2 group is very close to the C(1)H_2–C(2)H part: C(1)···C(14), 2.87(2); C(2)···C(14), 3.17(2) Å. The difference of 5° between the C(6)–C(7)=C(14) and C(8)–C(7)=C(14) bond angles probably results from this steric repulsion. The Cl atom is gauche to both the Br(1) atom and the C(15)H_3 groups: Cl···Br(1), 3.430(4); Cl···C(15), 3.19(1) Å. These gauche interactions cause the C(3)–C(2)–Cl bond angle to be greater than the C(1)–C(2)–Cl angle by 4°. A similar bond-angle distortion is found also for the C(3)–C(15) bond; the C(2)–C(3)–C(15) angle is greater than the C(4)–C(3)–C(15) angle by 5°. On the other hand, in spite of the severe steric hindrance between the Cl and Br(1) atoms, the C(2)–C(3)–Br(1) bond angle is smaller than the tetrahedral angle, and is almost equal to the C(4)–C(3)–Br(1) and C(15)–C(3)–Br(1) angles. As was pointed out in a previous paper,[7] such a shrinkage of the C–C–halogen bond angles seems likely to be a property of tertiary chlorides and bromides.

The C(5)H_2 and C(13)H_3 groups are placed axially on the B-ring, while the Br(2) atom and the C(1)H_2 and C(12)H_3 groups are equatorially oriented. The Br(2) atom suffers gauche repulsions from both C(12)H_3 and C(13)H_3 groups: Br(2)···C(12), 3.23(1); Br(2)···C(13), 3.31(1) Å. Consequently, the C(11)–C(10)–Br(2) bond angle is greater than the C(9)–C(10)–Br(2) angle by 5°. The C(6)–C(11) distance is considerably longer than the standard C–C single-bond distance. Since both of the C(6) and C(11) atoms have three bulky groups, this bond lengthening is probably due to strong steric repulsions among these groups.

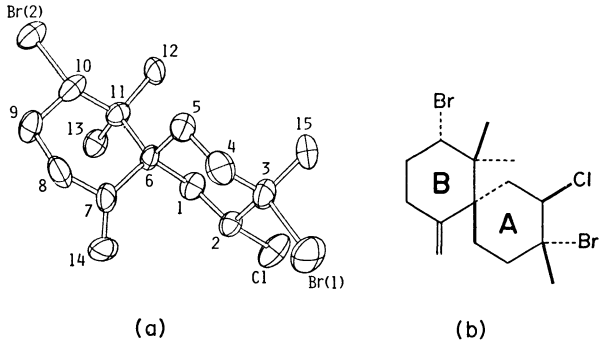

Fig. 1. (a) A perspective view of the **1** molecule, and (b) the corresponding structural formula. Each non-hydrogen atom is represented as a thermal ellipsoid enclosing a 50% probability. The symbol C for carbon atoms is omitted.

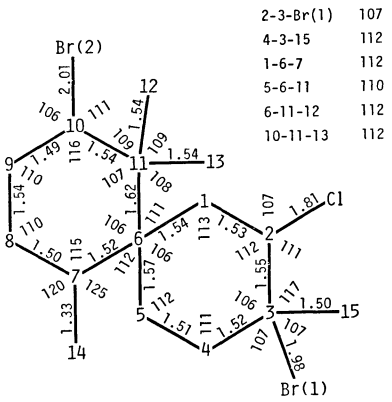

Fig. 2. The bond distances (l/Å) and angles (θ/°). The e.s.d.'s are 0.01—0.02 Å and 0.7—1.1° respectively.

References

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