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X-RAY CRYSTAL STRUCTURES AND CONFORMATIONS OF 6β,12β-DIHYDROXY-3*E*,7*E*-DOLABELLADIENE 6-*p*-BROMOBENZOATE AND ACETOXYODONTOSCHISMENOL 3S,4S-EPOXIDE

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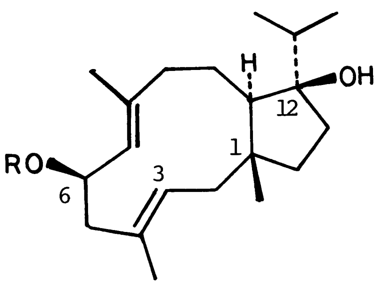
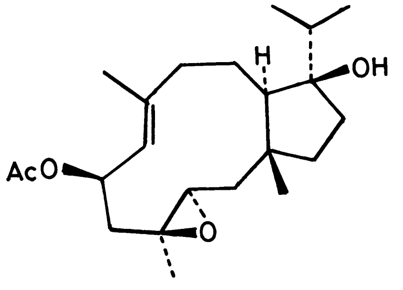
The structures and conformations of 6β,12β-dihydroxy-3*E*,7*E*-dolabelladiene 6-*p*-bromobenzoate and acetoxyodontoschismenol 3S,4S-epoxide have been established by X-ray crystallographic analysis. The original assignment of the stereochemistry at C-12 of (+)-acetoxyodontoschismenol has been revised.

Recently we proposed the structure and absolute configuration of the antifungal dolabellane diterpenoid, (+)-acetoxyodontoschismenol, from the liverwort, *Odontoschisma denudatum* (Nees) Dum.[1,2] We now describe the results of crystal structure analyses of two derivatives, the 6-*p*-bromobenzoate (**2**) and the 3S,4S-epoxide (**3**), of (+)-acetoxyodontoschismenol which confirm its structure as 6β-acetoxy-12β-hydroxy-3*E*-7*E*-dolabelladiene (**1**) with a revised configuration at C-12. The crystal conformations of **2** and **3** are essentially the same as that proposed for **1** on the basis of NMR arguments.[1)]

The 6-*p*-bromobenzoate (**2**), mp 67-68 °C,[1)] was readily prepared from the deacetoxyl derivative (**4**) of **1**. The crystallographic data are as follows: $C_{27}H_{37}BrO_3$, M=489.5, monoclinic, space group A2, a=20.044(6), b=8.192(4), c=17.023(7) Å, β=94.15(5)°, U=2788 Å^3, Z=4, Mo-Kα radiation λ=0.7107 Å. X-Ray intensities were measured on an Enraf-Nonius CAD4 diffractometer for 2729 reflections with $2\theta < 50^\circ$ and these gave 1740 unique reflections with $I > 2.5\sigma(I)$. The position of the bromine atom was determined from a Patterson synthesis, and the carbon and oxygen atoms were located by Fourier syntheses. After preliminary least-squares refinement, the hydrogen atoms were located in a difference electron-density distribution and were included in subsequent calculations at fixed positions. Disordered solvent was revealed in one region of the difference electron density distribution and several peaks were treated as carbon atoms with variable occupation parameters. In the final refinement stage the absolute configuration was established by refinement of the η parameter.[3)] At convergence, R=0.068, R_w=0.098 with weights given by $w=1/\sigma^2(|F|)$. In view of the disordered



1 R=Ac
2 R=p-BrC_6H_4CO
4 R=H



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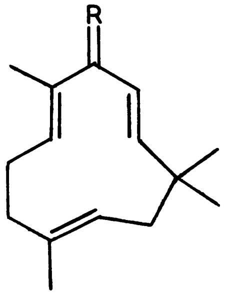
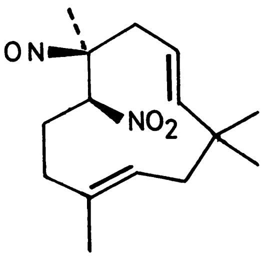


5 R=O
8 R=H_2



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solvent, a second batch of crystals was prepared and a new data set measured on another CAD4 diffractometer. In this case 2733 reflections with $2\theta \leqslant 50^\circ$ gave 1801 unique reflections with $I > 2.5\sigma(I)$. Least squares calculations converged at $R=0.061$, $R_w=0.075$, again with disordered solvent, and confirmed the absolute confoguration.[4] The crystallographic calculations were performed with the GX package.[5,6] The molecular structure in the correct absolute configuration is shown in Fig. 1. These results confirm the previously proposed structure of (+)-acetoxyodontoschismenol with the exception of the configuration at C-12.[1] The tertiary hydroxyl group was originally assigned the α configuration on the basis of insignificant solvent and lanthanide-induced shifts of the tertiary methyl group. It is clear from the Fig. 1 that the pseudo-equatorial nature of the tertiary hydroxyl group accounts for the failure to observe bigger shifts.

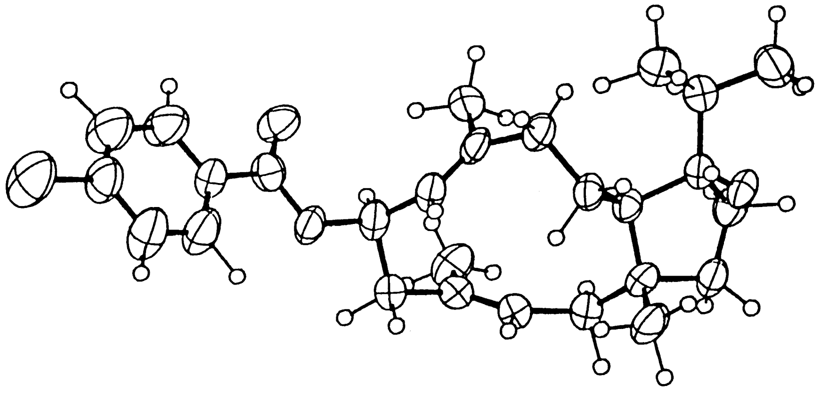

Fig. 1. A perspective view of the molecule (2).

The crystallographic data for the 3S,4S-epoxide (3), $C_{22}H_{36}O_4$, mp 104-105 °C,[1] are as follows: orthorhombic, space group $P2_12_12_1$, $a=8.527(1)$, $b=13.598(3)$, $c=36.592(9)$ Å, $U=4243$ Å^3, $Z=8$, $D_c=1.14$ g cm^{-3}. The diffraction intensities with $2\theta \leqslant 50^\circ$ were collected in a variable speed ω scan mode using graphite monochromated Mo-Kα radiation (λ=0.7107 Å) on a Syntex R3 four-circle diffractometer.

Of 4252 independent reflections, 3048 having $Fo \geqslant 2\sigma(Fo)$ were judged to be observed after correction for Lorentz, polarization, and background effects. The structure was solved by the direct method MULTAN 78,[7] and refinement by the full-matrix least-squares using anisotropic thermal parameters for the non-hydrogen atoms and isotropic ones for the hydrogen atoms was performed with UNICS III program system.[8] The final R value was 0.077.[4] The structure of the 3S,4S-epoxide (3) is shown in Fig. 2.

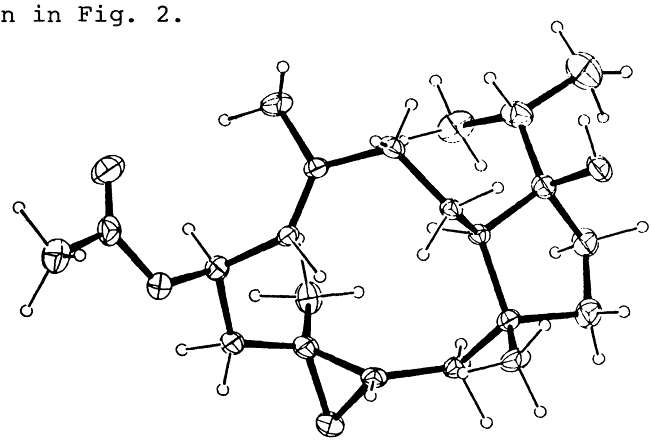

Fig. 2. A perspective view of the molecule (3).

The eleven-membered ring has essentially the same conformation in the *p*-bromobenzoate (2) and the epoxide (3). This conformation has been previously observed in zerumbone (5)[9] and humulene nitrosite (6)[10] and represents the minimum energy form of cycloundeca-1,5-diene (7) as indicated by extensive molecular mechanics calculations for a range of conformations using the White and Bovill force field.[11] The torsion angles for these compounds are compared in Table 1. The conformation also corresponds to the CC conformation calculated for the sesquiterpene humulene (8) by Shirahama *et al.*[12]

Table 1. Torsion angles of the cycloundecadiene derivatives

	2	3	5	6	7	8
1-2-3-4	132	114	107	115	119	110
2-3-4-5	-175	-161	-167	-177	-177	-174
3-4-5-6	103	94	105	112	104	105
4-5-6-7	-62	-45	-46	-53	-56	-45
5-6-7-8	110	131	141	110	100	125
6-7-8-9	-167	-174	-168	-164	-171	-174
7-8-9-10	64	34	26	67	78	45
8-9-10-11	71	64	52	63	64	58
9-10-11-1	-147	-153	-172	-160	-151	-175
10-11-1-2	96	118	136	99	100	121
11-1-2-3	-62	-65	-48	-56	-57	-44

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6) For the determination of absolute configuration, values of anomalous dispersion components were taken from International Tables for X-Ray Crystallography, Vol. 3, and the parameter η was initially assigned the value +1. At convergence, the final value of η was -0.57(13) for the first data set and -0.46(10) for the second. Both values are significantly negative and indicate that the absolute configuration is opposite to that arbitrarily chosen by the initial solution of the crystal structure. The absolute configuration specified by the calculations agrees with that deduced earlier for (+)-acetoxyodontoschismenol and is incorporated in Fig. 1, the torsion angles of Table 1 and the deposited co-ordinates.
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