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8-Desacetoxy-11βH,13-dihydroperoxyferolide, a Sesquiterpene Lactone Hydroperoxide

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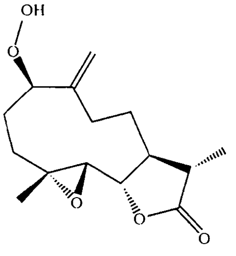
Abstract

The γ-lactone of $C_{15}H_{22}O_5$ has an envelope conformation with the β-carbon at the flap. The hydroperoxy group is disordered with 92% R configuration and 8% S configuration at the chiral center to which it is bonded. The O—O distance for the major configuration is 1.463 (3) Å. Intermolecular hydrogen bonding exists between the hydroperoxy group and the carbonyl oxygen, with the major configuration having an O···O distance of 2.742 (3) Å.

Comment

The biosynthesis of hydroperoxy sesquiterpene lactones is believed to involve chlorophyll-mediated singlet oxygen oxidation of the 1,10-double bond of the corresponding germacrolides (Denny & Nickon, 1973). To investigate this procedure, the title compound, (I), was synthesized by *in vitro* singlet-oxygen photooxygenation of dihydroparthenolide (Pentes, 1991). The crystal structure of (I) was determined in order to discover its identity and stereochemistry.



(I)

The γ-lactone of the structure of (I) is present in an envelope conformation with C7 in the flap position. This conformation is common in sesquiterpene γ-lactones containing a methyl group at the α position of the lactone (Castañeda-Acosta et al., 1998). Torsion angles for the ten-membered ring are given in Table 1. Comparison of the ten-membered ring of the title compound with that of the starting material, dihydroparthenolide (Rugutt et al., 1997), shows that only conformations about the C3—C4, C4—C5 and C5—C6 bonds were retained. A search of the Cambridge Structural Database (Allen & Kennard, 1993) for sesquiterpene lactones with a similar ten-membered-ring conformation failed to locate pertinent structures. The hydroperoxy group of the molecule is disordered, with 92% β-orientation and 8% α-orientation, indicating that two diastereomers formed in the reaction and co-crystallized. The C1 stereocenter thus exists in both R and S configurations, with the R configuration predominant in the crystal. The other five stereocenters of the molecule have configurations C4(R), C5(S), C6(S), C7(R) and C11(S). The O4A—O5A distance, 1.463 (3) Å, agrees well with the expected value of 1.464 Å (Allen et al., 1987). The C1—O4A—O5A angle of 104.9 (1)° deviates significantly from the expected value of 108.2° (the average of nine values taken from the Cambridge Structural Database; refcodes CERCEH, CIHZEY, CUHZAG, DAWCAF, DAWCAF10, KEDDOM, TABLUD, VUYXES, YAWXOJ). We attribute this to probable unresolved disorder in C1, which would be expected to occupy slightly different positions in the α and β isomers. The observed C1—O4B—O5B angle of 91 (1)° and O4B—O5B distance of 1.54 (2) Å are not considered reliable, but are artifacts resulting from the disorder and the low population of this configuration. Intermolecular hydrogen bonding exists between the disordered O5 atoms of the hydroperoxy group and the carbonyl oxygen of the γ-lactone. The O5A···O3^i and O5B···O3^i distances are 2.742 (3) and 2.97 (3) Å, respectively [symmetry code: (i) $1+x$, y, $1+z$]. The O5A—H···O3^i angle is 150 (3)°.

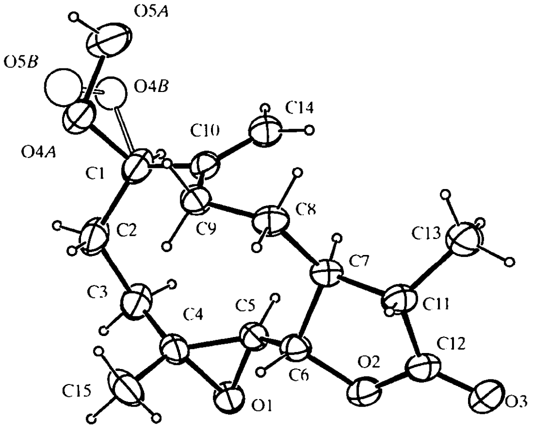


Fig. 1. The title molecule with displacement ellipsoids plotted at the 30% probability level. The minor sites of the hydroperoxy O atoms are illustrated as open circles.

Experimental

A 300 mg sample of dihydroparthenolide and 10 mg of methylene blue were dissolved in 30 ml of dichloromethane.

Oxygen was bubbled through the solution at a temperature of 288–298 K for 4 h while it was irradiated with visible light from a tungsten-filament lamp placed 15 cm from the flask. The product was separated from the reaction mixture by vacuum liquid chromatography, eluting with ethyl acetate. Crystals were grown by evaporation of the solvent.

Crystal data

$C_{15}H_{22}O_5$
$M_r = 282.34$
Triclinic
$P1$
$a = 5.7473\ (3)$ Å
$b = 7.6109\ (7)$ Å
$c = 9.0705\ (9)$ Å
$\alpha = 70.190\ (8)°$
$\beta = 85.259\ (6)°$
$\gamma = 78.188\ (6)°$
$V = 365.34\ (6)$ Å^3
$Z = 1$
$D_x = 1.283$ Mg m^{-3}
D_m not measured

Cu $K\alpha$ radiation
$\lambda = 1.54184$ Å
Cell parameters from 25 reflections
$\theta = 23–38°$
$\mu = 0.75$ mm^{-1}
$T = 296$ K
Prism
0.38 × 0.23 × 0.12 mm
Colorless

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: ψ scans (North *et al.*, 1968)
$T_{\min} = 0.78$, $T_{\max} = 0.91$
2951 measured reflections
2951 independent reflections (including Friedel pairs)

2924 reflections with $I > 0$
$\theta_{\max} = 75°$
$h = -7 \rightarrow 7$
$k = -9 \rightarrow 9$
$l = -11 \rightarrow 11$
3 standard reflections
frequency: 120 min
intensity decay: 2.5%

Refinement

Refinement on F^2
$R(F) = 0.040$
$wR(F^2) = 0.054$
$S = 1.94$
2924 reflections
194 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 4F_o^2/[\sigma^2(F_o^2) + 0.0004F_o^4]$
$(\Delta/\sigma)_{\max} = 0.02$
$\Delta\rho_{\max} = 0.25$ e Å^{-3}
$\Delta\rho_{\min} = -0.24$ e Å^{-3}

Extinction correction: isotropic (Zachariasen, 1963)
Extinction coefficient: $1.5\ (2) \times 10^{-5}$
Scattering factors from *International Tables for X-ray Crystallography* (Vol. IV)
Absolute structure: assumed to correspond to the accepted absolute configuration of sesquiterpene lactones from higher plants (Fischer *et al.*, 1979)

Table 1. *Selected geometric parameters (Å, °)*

O1—C4	1.453 (2)	O5*A*—H5O	1.01 (4)
O1—C5	1.433 (2)	C4—C5	1.473 (2)
O4*A*—O5*A*	1.463 (3)	C10—C14	1.317 (2)
O4*B*—O5*B*	1.54 (2)	C11—C13	1.507 (3)
O4*A*—C1	1.458 (3)		
C4—O1—C5*A*	61.34 (8)	O4*A*—C1—C10	109.6 (2)
O5*A*—O4*A*—C1	104.9 (1)	O1—C4—C5	58.7 (1)
O4*A*—O5*A*—H5O	92 (2)	O1—C5—C4	60.01 (9)
O4*A*—C1—C2	100.6 (2)	C1—O4*B*—O5*B*	91 (1)
C12—O2—C6—C7	23.6 (2)	C5—C6—C7—C8	81.0 (2)
C6—O2—C12—C11	−2.1 (2)	C6—C7—C8—C9	−54.8 (2)
C2—C1—C10—C9	−49.0 (2)	C7—C8—C9—C10	−54.5 (2)
C1—C2—C3—C4	85.1 (2)	C8—C9—C10—C1	163.8 (2)
C2—C3—C4—C5	−98.2 (2)	C8—C9—C10—C14	−22.1 (3)
C3—C4—C5—C6	147.8 (2)	C7—C11—C12—O2	−20.1 (2)
C4—C5—C6—C7	−113.2 (2)	C7—C11—C12—O3	159.1 (2)
O2—C6—C7—C11	−34.7 (2)		

The minor sites O4*B* and O5*B* of the disordered O atoms of the hydroperoxy group were refined with isotropic displacement parameters. The populations of the disordered O sites were estimated by individual refinement of their multiplicities. In the final cycles, they were fixed at *A*:*B* = 92:8, which yielded reasonable displacement parameters. The H atoms on C5 and O5*A* were refined isotropically, with $B_{\rm iso}$ fixed at 10 Å^2 for the latter. All other H atoms were placed in calculated positions, guided by difference maps, with C—H 0.95 Å and $B_{\rm iso} = 1.3B_{\rm eq}$ for the bonded C atom. The H atom on O5*B* was not located. Refinement of the reported (and expected) configuration yielded $R = 0.0402$, $wR = 0.0530$ and $S = 1.939$, while refinement of the enantiomer yielded $R = 0.0404$, $wR = 0.0543$ and $S = 1.956$.

Data collection: *CAD*-4 *Operations Manual* (Enraf–Nonius, 1977). Cell refinement: *CAD*-4 *Operations Manual*. Data reduction: *PROCESS* in *MolEN* (Fair, 1990). Program(s) used to solve structure: *MULTAN*80 (Main *et al.*, 1980) (direct methods). Program(s) used to refine structure: *LSFM* in *MolEN*. Molecular graphics: *ORTEP*II (Johnson, 1976). Software used to prepare material for publication: *BTABLE PTABLE CIF IN* in *MolEN*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SX1065). Services for accessing these data are described at the back of the journal.

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Nitro Derivatives of 3-Acetamidobenzyl Acetate

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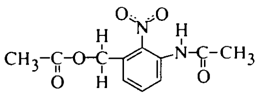
Abstract

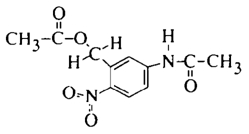
The structures of 3-acetamido-2-nitrobenzyl acetate, $C_{11}H_{12}N_2O_5$, (I), 3-acetamido-6-nitrobenzyl acetate, $C_{11}H_{12}N_2O_5$, (II) and 3-acetamido-6-nitrobenzyl acetate monohydrate, $C_{11}H_{12}N_2O_5.H_2O$, (III), have been determined at low temperature; 150 K for (I) and (III), and 100 K for (II). The molecules differ mainly in the conformation of the acetamide and acetate groups with respect to the aromatic ring plane: in (II) they are almost coplanar, in (I) they are markedly distorted from planarity, while in (III) they are intermediate. The nitro group is twisted with respect to the aromatic ring in (I), but is almost coplanar with it in (II) and (III). In all three structures, one of the nitro O atoms is directed towards a methylene C atom, approximately bisecting the H—C—H angles, and intramolecular C—H···O hydrogen bonds involving the aromatic H and carboxyl O atoms are observed. In all three cases, the crystal structures are stabilized by intermolecular N—H···O [and O—H···O in (III)], as well as weak C—H···O, hydrogen bonds.

Comment

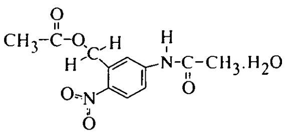
The electronic structure of nitrobenzene and its substituted derivatives has been the subject of longstanding interest for organic chemists. Conjugation between the nitro group and the aromatic system was suggested many years ago (Trotter, 1960). In recent years, many spectroscopic, structural and theoretical studies have shown that the quinoidal structure plays only a minimal role in the resonance structures (Butcher *et al.*, 1991; Vinson & Dannenberg, 1989; Bromilow *et al.*, 1980; Hiberty & Ohanessian, 1984). On the other hand, it is well known that the position of the nitro group in a nitrobenzene carrying one or more different substituents could strongly influence the conformation of the rest of the molecule (Butcher *et al.*, 1992). This paper describes two structural isomers of 3-acetamidobenzyl acetate with the nitro groups in positions 2 or 6. The structure of the 4-nitro isomer has been described previously (Rusek *et al.*, 1995).



(I)



(II)



(III)

The structures presented differ only in the position of the nitro group on the aromatic ring. Compound (III) is the monohydrate of compound (II). The molecules each have three different substituents connected to the benzyl skeleton, namely nitro, acetamido and acetate groups (Figs. 1, 2 and 3). In all three structures, the bond lengths in the aromatic and aliphatic parts are comparable within 3σ and similar to other aromatic nitro compounds (Allen *et al.*, 1991). The most significant difference observed is for the C4—C5 bond length [1.364 (4) Å in (II), but 1.386 (3) and 1.381 (2) Å in (I) and (III), respectively]. The bond angles are slightly different for all the structures, the biggest difference being observed for C2—C3—N1 [123.7 (2), 123.3 (3) and 115.8 (3)°, in (I), (II) and (III), respectively], probably as a result of the steric hindrance [in (I) and (II)] of the neighbouring nitro and acetamide groups in the aromatic ring. The widening of the C—C—N(amine) bond angle has been observed previously for other *o*-nitro amide aromatic compounds where the amide H atom is not involved in the intramolecular hydrogen bond (Allen *et al.*, 1991). In (III), the lower value of this angle is probably a consequence of the water molecule. The aromatic ring is slightly distorted from strict planarity, especially in (II), being slightly boat shaped, with C3 and C6 as the 'bows'; the largest deviation [0.021 (2) Å] from an aromatic ring plane occurs for C6 in (II).