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[3a*R*-(3aα,4α,7α,7aα)]-2-Acetyl-4,8,8-trimethylperhydro-4,7-methano-1,2-benzisoselenazol-3a-ol

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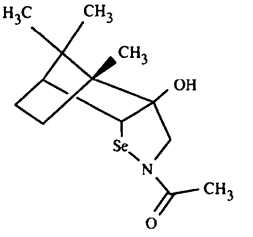
Abstract

Crystals of the title compound, $C_{13}H_{21}NO_2Se$, are composed of independent molecules wherein the six-membered ring of the camphor-derived moiety is fused with a novel five-membered heterocyclic ring incorporating Se and N atoms. The bond lengths and angles are normal, with Se—N and Se—C distances of 1.865 (3) and 1.943 (3) Å, respectively, and an N—Se—C angle of 87.1 (2)°. The mean value of the C_{sp^3}—C_{sp^3} bond length in the camphor moiety is 1.542 (15) Å. The five-membered ring has an N-envelope conformation and the molecules are hydrogen bonded forming chains extended along the *b*-axis direction, with O···O and O—H···O separations of 2.769 (4) and 1.84 Å, respectively.

Comment

Glutathione peroxidase (GSH–Px) is a selenium-containing enzyme that catalytically destroys hydroperoxides formed as normal by-products of oxidative metabolism (Hoekstra, 1974; Shamberger, 1983; Burk, 1994; Tappel, 1984; Flohé, 1985). This protects living organisms from damage that ensues from free radicals that would otherwise be generated from such hydroperoxides. It has been established that the redox properties of selenocysteine residues in GSH–Px are responsible for its catalytic activity (Ganther, 1975; Ganther & Kraus, 1984). A variety of simpler synthetic selenium and tellurium compounds have been investigated for similar abilities to destroy peroxide species (Reich & Jasperse, 1987; Wilson *et al.*, 1989; Iwaoka & Tomoda, 1994; Engman *et al.*, 1992; Engman, Stern *et al.*, 1994; Vessman *et al.*, 1995; Engman, Andersson *et al.*, 1994; Detty *et al.*, 1994; Fong & Schiesser, 1995; Jacquemin *et al.*, 1992; Galet *et al.*, 1994). One such compound, Ebselen, has been studied for its therapeutic potential as an anti-inflammatory agent, and in connection with a variety of other disease states related to oxidative stress and ensuing free-radical formation (Fong & Schiesser, 1995; Jacquemin *et al.*, 1992; Galet *et al.*, 1994). Ebselen and related compounds, however, function by mechanisms that are significantly different from that of GSH–Px itself (Engman *et al.*, 1992; Fischer & Dereu, 1987; Haenen *et al.*, 1990).

We recently reported that the novel (1*R*)-(+)-camphor-derived cyclic selenenamide (1) catalytically destroys hydroperoxides *via* an identical mechanism to that used by GSH–Px (Back & Dyck, 1997). Since it is of interest to design and test structural variations of GSH–Px mimetic (1) in attempts to improve its catalytic properties, it is important to know the precise structure of this lead compound. In connection with our efforts in this area, we now report the structure and absolute configuration of (1) determined by X-ray crystallography.



(1)

The title compound (Fig. 1) contains a novel five-membered heterocyclic ring containing Se and N atoms, which is being reported for the first time in a crystal structure, fused with the six-membered ring of a camphor-derived moiety. A search of the Cambridge Structural Database (Allen & Kennard, 1993) did not reveal any structure containing the heterocyclic ring present in (1). The bond lengths and angles are normal, with Se—N and Se—C distances of 1.865 (3)

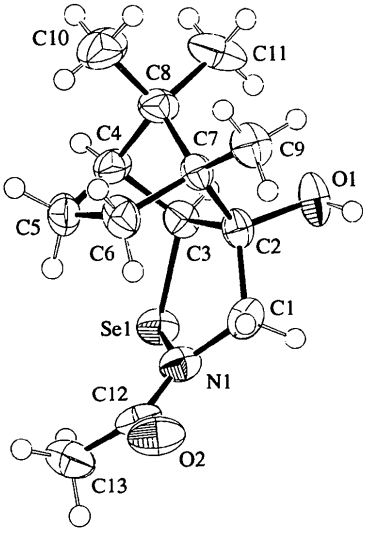


Fig. 1. *ORTEP*II (Johnson, 1976) drawing of the title compound. Displacement ellipsoids are plotted at the 50% probability level.

and 1.943 (3) Å, respectively, and an N—Se—C angle of 87.1 (2)° (Allen *et al.*, 1992). The mean value of the C_{sp^3}—C_{sp^3} bond length in the camphor moiety is 1.542 (15) Å, while the C_{sp^3}—C_{sp^2}, N—C_{sp^3}, N—C_{sp^2}, O—C_{sp^3} and O=C bond lengths are 1.496 (7), 1.463 (5), 1.348 (5), 1.425 (4) and 1.243 (4) Å, respectively. The five-membered ring has an N1-envelope conformation, with N1 0.619 (6) Å out of the plane of the remaining atoms of the ring. The selenenamido moiety comprised of the Se1, N1, O2, C1, C12, C13 atoms is almost planar, with a maximum deviation of 0.050 (5) Å. The molecules are linked in the solid by hydrogen bonds extending along the *b*-axis direction (details are in Table 2).

Experimental

The title compound was prepared according to a procedure described previously (Back & Dyck, 1997). Suitable crystals were grown by slow evaporation from an ether–hexane solution at room temperature.

Crystal data

$C_{13}H_{21}NO_2Se$
M_r = 302.27
Orthorhombic
$P2_12_12_1$
a = 6.8684 (10) Å
b = 11.537 (2) Å
c = 17.079 (3) Å
V = 1353.4 (4) Å^3
Z = 4
D_x = 1.483 Mg m^{-3}
D_m not measured

Cu $K\alpha$ radiation
λ = 1.54178 Å
Cell parameters from 25 reflections
θ = 20–30°
μ = 3.684 mm^{-1}
T = 293 (1) K
Needle
0.30 × 0.12 × 0.10 mm
Colorless

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: empirical *via* ψ scan of three reflections (North *et al.*, 1968)
T_{min} = 0.605, T_{max} = 0.692
2802 measured reflections
2466 independent reflections

2303 reflections with $I > 2\sigma(I)$
R_{int} = 0.049
θ_{max} = 68.0°
$h = 0 \rightarrow 8$
$k = 0 \rightarrow 13$
$l = -20 \rightarrow 20$
3 standard reflections every 200 reflections
intensity decay: 4.62%

Refinement

Refinement on F^2
$R(F)$ = 0.033
$wR(F^2)$ = 0.085
S = 1.107
2466 reflections
156 parameters
H atoms riding
$w = 1/[\sigma^2(F_o^2) + (0.05P)^2 + 0.5P]$ where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max}$ = 0.003
$\Delta\rho_{max}$ = 0.295 e Å^{-3}
$\Delta\rho_{min}$ = −0.529 e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for Crystallography* (Vol. C)
Absolute structure: Flack (1983)
Flack parameter = 0.03 (3)

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

Se1—N1	1.865 (3)	O2—C12	1.243 (5)
Se1—C3	1.943 (3)	N1—C12	1.348 (5)
O1—C2	1.425 (4)	N1—C1	1.463 (5)
N1—Se1—C3	87.1 (2)	C12—N1—Se1	126.4 (3)
C12—N1—C1	123.8 (3)	C1—N1—Se1	109.5 (3)

Table 2. *Hydrogen-bonding geometry (Å, °)*

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1—H1···O2^i	0.95	1.84	2.769 (4)	166

Symmetry code: (i) $-x, y - \frac{1}{2}, \frac{3}{2} - z$.

Data collection: *CAD-4 Software* (Schagen *et al.*, 1989). Cell refinement: *CAD-4 Software*. Data reduction: *TEXSAN* (Molecular Structure Corporation, 1994). Program(s) used to solve structure: *SAPI91* (Fan, 1991). Program(s) used to refine structure: *SHELXL93* (Sheldrick, 1993). Molecular graphics: *TEXSAN*. Software used to prepare material for publication: *SHELXL93*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: FG1405). Services for accessing these data are described at the back of the journal.

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1-Acetyl-2-thiohydantoin

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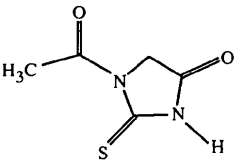
Abstract

In the title compound (1-acetyl-4-oxoimidazolidine-2-thione, $C_5H_6N_2O_2S$), the plane of the acetyl group forms an angle of 6.7° with the essentially planar thiohydantoin ring. N—H···O hydrogen bonds create quasi-planar chains of molecules along the *y* axis.

Comment

The structure of the title compound, (I), has been established as part of a study of the synthesis and characterization of metal complexes of 2-thiohydantoin and its derivatives (Casas *et al.*, 1995).



(I)

The molecular structure of (I) is shown in Fig. 1. The N1—C1—N2—C3—C2 ring and the peripheral S, C4 and O3 atoms define a plane (r.m.s. deviation 0.013 Å), as does the *N*-acetyl N1—C4(=O4)—C5 fragment (r.m.s. deviation 0.006 Å). The angle between the two planes is 6.7°.

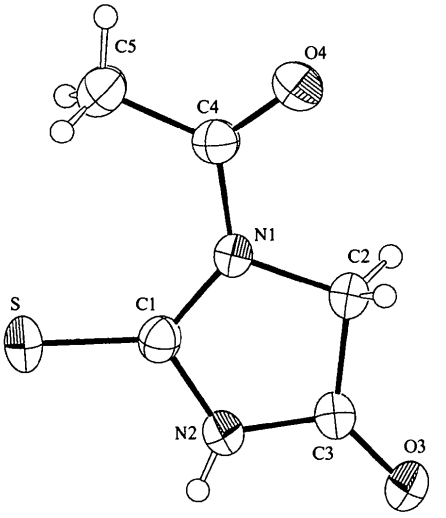


Fig. 1. The molecular structure of the title compound showing the atom-labelling scheme and 50% probability displacement ellipsoids.

The bond lengths and angles in the acetyl fragment are similar to those found in 1-acetyl-2-[1-(acetylthio)-ethyl]thiohydantoin (MacKay *et al.*, 1992), although in this C2-substituted thiohydantoin, the angle between the thiohydantoin ring and the acetyl group is 12°. In (I), the thiohydantoin ring bond lengths differing most from those found in 2-thiohydantoin (Devillanova *et al.*, 1987; Walker *et al.*, 1969) are those of C1—N1 and N1—C2, which are longer in the acetyl derivative. The internal ring angle most affected by *N*-acetylation is C2—N1—C1, which widens slightly to approximately the same value as in 1-acetyl-2-[1-(acetylthio)ethyl]thiohydantoin (MacKay *et al.*, 1992). *N*-Acetylation also affects the external angles flanking the C=S group, with N1—C1—S becoming wider and N2—C1—S narrower.

The N2—H2 bond and the O3 atom are involved in a hydrogen bond [N2—H2 0.77 (3), H2···O3^{i} 2.08 (4), N2···O3^{i} 2.849 (3) Å and N2—H2···O3^{i} 170 (3)°; sym-